A Review of the Efficiency of Interventions in HIV Infection, 1994-2003

Running Title: **Efficiency of Interventions in HIV Infection 1994-2003**

REVISED VERSION FOR THE JOURNAL DISEASE MANAGEMENT & HEALTH OUTCOMES 21st FEBRUARY 2005

Authors: Guy Harling
Department of Epidemiology and Biostatistics, McGill University, Montreal, Canada

Robin Wood
Desmond Tutu HIV Centre, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa

Eduard J. Beck
Department of Epidemiology and Biostatistics, McGill University, Montreal, Canada

Key words. **Cost-effectiveness, cost-utility, cost-benefit, HIV-related interventions**

Acknowledgements:

The authors would like to thank Professor Lee Soderstrom who made numerous insightful comments on drafts of the paper, and Laurie Tesseris for her patience and organisational assistance.

This work was supported by an unrestricted grant from *Secure the Future*

Name and Address for Correspondence:

Dr Eduard J. Beck
Strategic Information and Research (SIR) Unit,
HIV Department, HIV-Tuberculosis-Malaria Cluster,
World Health Organization,
20 Avenue Appia, 1211 Geneva 27, Switzerland.
Phone: ++ 41 22 791 5521; Fax: ++ 41 22 791 4834;
Email: becke@who.int; eduard.beck@mcgill.ca

The final publication is available at Springer via http://dx.doi.org/ 10.2165/00115677-200513060-00003.

Table of Contents:

Table of Tables:

Figures:

Abbreviations

3TC	Lamivudine
AIDS	Acquired ImmunoDeficiency Syndrome
ART	Anti-RetroViral Therapy
CAESAR	The Canada, Australia, Europe, South Africa study
CA	Cases Averted
CBA	Cost-Benefit Analysis
CEA	Cost-Effectiveness Analysis
CMV	Cytomegalovirus
CTRPN	Counselling, Testing, Referral and Partner Notification
CUA	Cost-Utility Analysis
DALY	Disability-Adjusted Life Years
DOTS	Directly Observed Treatment, Short-course
ELISA	Enzyme-Linked ImmunoSorbent Assay
HAART	Highly Active Anti-Retroviral Treatment
HIV	Human Immunodeficiency Virus
ICER	Incremental Cost-Effectiveness Ratio
IDU	Intravenous Drug User
ID	Infection Detected
LYG	Life Year(s) Gained
MAC	Mycobacterium Avium Complex
MSM	Men who have Sex with Men
MTCT	Mother To Child Transmission
NEP	Needle Exchange Programme
NICE	National Institute for Clinical Excellence
NVP	Nevarapine
OI	Opportunistic Infection
PCP	*Pneumocystis carinii* Pneumonia
PEP	Post-Exposure Prophylaxis
PCR	Polymerase Chain Reaction
PI	Protease Inhibitor
QALY	Quality-Adjusted Life Years
STD	Sexually Transmitted Disease
TMP-SMX	Trimethoprim-Sulfamethoxazole
VCT	Voluntary Counselling and Testing
WB	Western Blot
WHO	World Health Organisation
ZDV	Zidovudine

Abstract:

HIV/AIDS is the fastest-growing health problem in the world today. Given the limited resources available to the healthcare system in many of the most heavily affected countries it is crucially important to know the effectiveness, efficiency, equity and acceptability of the interventions being considered to contain this pandemic. This review examined the peer-reviewed literature on the efficiency of prevention, treatment and care interventions published between 1994 and 2003, findings reported by these studies and methods used. The results varied by geographical setting and population studied. Some interventions were clearly cost-effective: prevention efforts and testing programmes among vulnerable populations; blood screening in high-income nations and in sub-Saharan Africa; providing anti-retroviral drugs and other interventions to expectant mothers and infants; treating certain opportunistic infections; and providing combination anti-retroviral therapy. However, most studies were set in the USA, while only one in six dealt with sub-Saharan Africa. No studies could be identified from Asia, Latin America or Eastern Europe. Three-quarters of all papers focused on hospital or primary care settings, with only a few prevention studies evaluating community-based interventions. Because of a paucity of primary data, outcomes or costs were frequently modelled, using data from multiple sources in the absence of context-specific data. Establishing multi-centre prospective monitoring systems on the use, cost and outcome of HIV service provision in middle- and lower income countries may provide data, to fill some of the large gaps, which exist in the literature on interventions in these countries. This results in gaps in the scientific literature, limiting its ability to guide policy-makers in those settings where the epidemic is most intense. Increased research in such settings and dissemination of their findings is urgently required, especially given the need for

intensified prevention strategies to complement the scaling up of HIV treatment and care services in these countries.

1. Introduction

The pandemic caused by the human immunodeficiency virus (HIV) is one of the greatest public health threats in the world today. It is estimated that 40 million HIV infected people were alive, while another 25 million are thought to have died of the illness by December 2003[1]. Five million people are thought to have been infected during the previous twelve months. The majority of the disease burden remains in sub-Saharan Africa, but the number of HIV infected people is rapidly increasing in other regions, especially in Asia and Eastern Europe.

HIV is predominantly transmitted sexually, but other routes of transmission include parenteral transmission – through infected blood, blood products or injecting drug use (IDU) – and vertical transmission from mother to child (MTCT), which may occur before, during or after birth. Although the complementary nature of preventing new HIV infections and treatment and care of HIV infected individuals was recognised some time ago,[2] only recently has it been more widely recognised that the containment of the HIV pandemic requires a global strategy which combines effective prevention with treatment and care programmes.[3] The provision of treatment and care to millions of HIV infected people has now become a major policy target among national and international organizations across the world. WHO and UNAIDS are now implementing the "3 by 5" programme, first announced at the Barcelona 2002 World AIDS Conference[4] with the aim of scaling up of HIV treatment and care in middle and low-income countries for

three million HIV infected individuals by the end of 2005. This is 50% of the estimated HIV infected people in the world who require such services.

Although this is an emergency response, to be successful in the longer term such programmes must be biomedically, economically, socially and politically sustainable, and need to strengthen local health services. The success of these programmes needs to be assessed in terms of their *effectiveness*, *efficiency*, *equity* of coverage and *acceptability* to both users and providers.[5] *Effectiveness* in this context refers to the outcome of interventions in real life situations; *efficiency* focuses on the level of resources required to achieve an outcome; *equity* considers the distribution of benefits from the intervention or programme; and *acceptability* can refer to the intervention being acceptable to users and providers, or the quality of life improvements achieved through it.[5] This is particularly important given the limited resources available in those countries most affected by the pandemic.[5]

While all four criteria are important, this paper reviews only the literature on the efficiency of HIV-related interventions, published in the Anglo- or Francophone scientific literature. The studies cover HIV prevention, HIV testing and blood screening, mother to child transmission, and HIV treatment and care including anti-retroviral therapy (ART) and opportunistic infections (OIs). The literature was evaluated using two criteria: the topics covered and the methodological strength of the studies, where this strength was judged on the type of data used, the clarity of the explanation provided and the degree of certainty with which the results were presented.

While most literature reviews to date have focused on interventions of particular types, or in certain geographic areas, this paper tries to provide a broad overview of the literature published between 1994 and 2003. This allows the identification of topics that have been well-studied and those that have been neglected during this period. It also permits comparisons of the relative efficiency and practicability of the full range of interventions and methodologies to be made.

2. Economic analysis

The key underlying principle of any economic analysis is the concept that using resources in one setting necessarily prevents them being used elsewhere, which is referred to as the 'opportunity cost' of the intervention. For example, should we spend resources on building a new hospital, these resources can not then be spent on renovating existing hospitals. While building new hospitals can provide benefits through new and improved services, the opportunity cost of this course of action comprises the additional benefits foregone, which would have been created through the improvement of services at existing sites. The desire to maximize outcomes makes consideration of opportunity costs essential.

Economic analyses should also aim to provide information that will allow policy makers to evaluate the sustainability of programmes. Cost studies provide information on the cost or affordability of a particular programme or intervention. Studies of the efficiency of interventions or programmes on the other hand provide information on the relative costs and benefits of a new intervention or programme, compared with existing alternatives.[5]

Three methods are commonly used to study the efficiency of new interventions or programmes: *cost-effectiveness*, *cost-utility* and *cost-benefit* analyses.[6] In *cost-effectiveness analyses* (CEA) costs are linked to a biological outcome, and the monetary resources required to achieve a unit of this outcome are evaluated. A commonly used outcome in studies assessing treatment and care is the number of 'life years gained' (LYG), whereas in preventive interventions, cases or infections averted are frequently used. While conceptually simple for most professionals to understand, difficulties may arise when one has to compare between different programmes using diverse outcome measures. For example, comparisons between the cost-effectiveness of treatment and preventive programmes to date have been difficult because of the different outcome measures used.

To address this problem, some health economists promoted the use of *cost-utility analyses* (CUA), where patient health states are given utility weightings, which are used to determine the number of life years gained through the intervention, adjusted for their quality of life. Costs are then linked to these adjusted outcomes, and instead of having to compare 'life years gained' with 'cases averted', comparisons can be made in terms of 'cost per adjusted life year'. This method therefore provides comparability across diseases or intervention categories, but often relies on quality-adjusted life years (QALYs), which are based on the preferences of specific individuals from a particular culture at a single point in time. In addition, some professionals question whether complex disease states can be really reduced into a single numerical figure between 0 and 1. A second, very similar, CUA outcome measure promoted in recent years by WHO is the disability-adjusted life year (DALY).[7] This measure focuses on the ability of

patients to perform various daily activities, while the QALY takes a somewhat more subjective approach, also valuing mental well-being.[8]

Some policy makers, including ministers of finance and treasury officials, would like to compare the impact of programmes from different government departments, where intervention outcomes cannot only be measured in terms of QALYs or other disaggregated measures. In this situation *cost-benefit analyses* (CBA) are used, where the outcome of the intervention or programme is also expressed in monetary terms. This approach allows for the impact of these interventions to be estimated across highly diverse settings, however translating biological or other outcomes into monetary terms can also be problematic.

Two other methodologies are sometimes used to assess the relative costs and benefits of an intervention. *Cost-minimisation analyses* are a specific form of CEA or CUA, involving interventions of similar effectiveness but different costs, and seeking to find the least expensive way to achieve the outcome. *Threshold analyses* on the other hand focus on determining how much an intervention would need to cost in order to be cost-saving or cost-effective, given that the outcome of that intervention is known. Neither c*ost-minimisation analyses* nor *threshold analyses* were included in the review.

Common to all these measures of efficiency is that they ask what improvement in outcome is found for the cost of the intervention or programme. This can be measured in terms of the absolute cost and outcome gain of an intervention – comparing it to no intervention – which produces an absolute cost-effectiveness ratio, or in terms of the change in cost and outcome of a new intervention relative to an existing one, which

produces an incremental cost-effectiveness ratio (ICER). It is important to be aware of which comparison is being made in a given study in order to understand what the result means. For brevity, the exact nature of the comparison made is not always specified in the text of the article, while full details of all comparisons cited are provided in the tables.

The lower the cost-effectiveness ratio is, the more efficient the new intervention can be considered to be. This cost-effectiveness may be measured relative to other interventions ("*X* is more/less cost-effective than *Y*"), or relative to a generalised cut-off based on the values and norms operative in a particular society ("*X* is cost-effective in the USA"). This cut-off at which an intervention may be considered 'cost-effective' should reflect what a given society is willing to pay for a particular policy at a particular point in time, but is often an arbitrary figure. In the USA it has been argued that interventions with ratios of less than $50,000 per QALY are usually considered cost-effective, and those with ratios of over $180,000 per QALY rarely are.[9] In the UK the National Institute for Clinical Excellence (NICE) uses a cut-off point of £30,000 ($48,990) per QALY or other outcome measure.[5] Such cut-off points can become unreasonably rigid however – for example, in Canada a cut-off of Can$20,000 ($14,270) was suggested in the early 1990's and is still being quoted today.[10,11]

For middle- and low-income countries,[12] a number of additional cut-off points have been suggested over the last decade. In the 1993 World Development Report, it was suggested that interventions with a cost of less than $50 per DALY saved could be considered highly cost-effective. The Commission on Macroeconomics and Health recently suggested that any intervention with a cost per DALY below the per capita income of a region should be considered highly cost-effective.[13] Finally some

economists have suggested a cut-off of twice the per-capita income of a country per outcome measure for those middle – or lower income countries which do not have accepted cut-off points. [14]

3. Methods

To be included in this review, articles had to have been peer-reviewed and published in English or French since 1994 and contain an analysis of costs linked to outcomes for an HIV-related intervention. Articles published prior to 1994 were included where their subject matter remained relevant. Papers dealing with voluntary counselling and testing (VCT), treatment and prophylaxis of opportunistic infections, community interventions to reduce high-risk behaviours and some blood screening programmes, were reviewed. Studies published before 1994 dealing with compulsory HIV testing, contact notification programmes and prophylaxis or treatment of HIV with zidovudine (ZDV) monotherapy, were excluded. The cut-off of 1994 was chosen to include the period during which a combination of antiretroviral drugs were starting to be used for HIV treatment. The final database search was performed in September 2004.

For the review, the following databases were searched: *American College of Physicians Journal Club, AIDSline, Cochrane Controlled Trials Register, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness, Econlit, HealthSTAR* and *Medline* using the keywords: *HIV, HIV-1, HIV-2, HIV-seropositivity, HIV infections* or *AIDS*, and *cost-benefit analysis, cost-effectiveness analysis, cost-utility analysis* or *cost-minimization analysis*. Following up additional references found in original studies or other review articles augmented these searches. Twenty-three review

articles[15-37] on the cost-effectiveness of HIV-related issues were identified and their references were used to check that no papers were missed by the search.

The search included studies relating to adults, adolescents and children. While there were numerous articles based on studies in adults or adolescents, apart from those dealing with mother-to-child transmission, only one efficiency study relating to children was found. The studies were divided into five broad categories, which included:

i. HIV prevention studies;
ii. Testing of patients or screening of blood for HIV infection;
iii. Prevention of mother to child transmission;
iv. Prophylaxis or treatment with ART and related issues;
v. Prophylaxis or treatment of opportunistic infections.

Each study was assessed using 19 criteria (table I) to ensure consistency across the reviews. These criteria also provided a guide in evaluating the methodological strength of the studies, particularly in terms of collection and manipulation of cost and outcomes data. The results section discusses only the main results for each study, but aspects to which these results were particularly sensitive are reported in tables III-VII in order to provide a more comprehensive picture.

[*insert table I around here*]

Each study was evaluated as to their perspective: when the study considered only costs directly relating to the intervention being performed, it was be considered to have a *programme perspective*; if it included other healthcare costs not directly attributable to the intervention it had a *healthcare system perspective*; if it included lost productivity or other non-healthcare costs it was said to have a *societal perspective*. It should be noted that all studies were assessed in terms of their specific geographical, institutional and

temporal context. Some studies were conducted in a hospital environment, while others took place in the community, and yet others were school- or prison-based. The context of the study affects both the costs and benefits that were found, and studies that failed to take a specific setting into account when modelling the impact of an intervention were likely to be less robust than those that did. Costs reported in the text were converted into US dollars, using January 2004 conversion rates, in addition to the original currency used in the study.

Finally, based on the criteria in Table I, all 175 studies included in the review were independently scored by two of the authors (GH and EJB) to assess their methodological strength and to reduce intra- and inter-observer variability. Studies for which the scores differed by more than four points were re-scored together by them. Scores for the studies in the five study categories were aggregated and for each category the mean score and 95% confidence intervals (CIs) calculated.

4. Results

A total of 1172 references were found. Of these, 175 articles matched the inclusion criteria and fell into five broad categories (table II). Thirty (18%) of the articles dealt with interventions carried out in the community. Twenty-one articles published prior to 1994 were not reviewed.[38-58]. The five categories were subdivided into different types of interventions. [*insert table II around here*]

4.1. HIV Prevention Studies

A total of 36 articles dealt with adolescent and adult prevention studies (table III).[59-94] These comprised studies on IDUs, other vulnerable populations and general populations.

[*insert table III around here*]

4.1.1. Interventions to reduce unsafe injections

Six studies dealt solely with IDUs, while a further two papers considered the impact of improving syringe policies in hospital settings. Villari et al.[59] looked at needle exchange programmes (NEP) in Italy, and found a very low cost-effectiveness ratio of $1,040 per LYG. Holtgrave et al.[60] modelled a NEP in the US to be cost-saving from a healthcare system perspective until coverage rose above 80 per cent of the population. Models by Laufer[61] and by Gold et al.[62] both suggested that NEPs were cost-saving from a healthcare system perspective, and a Canadian observational study by Jacobs et al.[63] found that over the first year of its life, the cost of a NEP was Can$9,537 ($6,800) per case averted.

Studying the impact of methadone maintenance in reducing HIV infection, Zaric et al.[64] found that regardless of IDU seroprevalence rates such programmes provided considerable benefits both to IDUs and to the general population, with a cost-effectiveness ratio of around $10,000 per QALY saved.

Laufer and Chiarello[65] reported that various needle stick-prevention devices provided protection at a rate of between $790 and $1,574 per injury averted in an US hospital setting. Dziekan et al.[66] examined the benefits of world-wide single-use syringe provision and education, and reported that in every region of the developing world the

cost per DALY of the programme was lower than the region's average annual per capita income.

4.1.2. Interventions in other vulnerable populations

Four studies considered interventions among women at increased risk of HIV infection. Two US-based studies were based on randomised trials in a community setting. Chesson et al.[67] found condom skills training, although not other skills training sessions, to be cost-saving among vulnerable women attending an urban health clinic; Holtgrave and Kelly[68] reported that condom skills training had a cost-effectiveness ratio of $2,024. Using survey data and literature-based assumptions, Moses et al.[69] found that treating sexually transmitted diseases (STDs) and raising condom use among sex workers in Nairobi, Kenya cost just $12 per case averted on a programme basis, including infections avoided both by clients and client's sexual partners. Marseille et al.[70] reported that a distribution programme to provide female condoms for sex workers in Mpumalanga, South Africa had a low cost-effectiveness ratio, and was cost-saving from a healthcare system perspective.

Observational studies among men-who-have-sex-with-men (MSM) were studied by Pinkerton et al.,[71] Kahn et al.[72] and Tao and Remafedi.[73] The first two papers found that interventions focusing on lowering risk behaviour were cost-saving from a healthcare system perspective. The third reported that a personalised counselling and risk-education intervention cost $6,180 per QALY saved from a healthcare perspective, but that it was cost-saving if lost productivity costs were included. Using data derived from a randomised trial, Holtgrave and Kelly[74] and Pinkerton et al.[75] reported that skills and

behaviour education were cost-effective from a programme perspective and cost-saving from a healthcare perspective.

Johnson-Masotti et al.[76] and Pinkerton et al.[77] studied randomised trials involving mentally ill adults, finding relatively high cost-effectiveness ratios for group risk-reduction interventions – from $40,000 to $136,000 per QALY. Both also reported substantial differences in response to the intervention by gender – in one case women were marginally responsive to risk reduction interventions,[76] in the other men did not change their behaviour at all.[77]

Sweat et al.[78] studied a randomised trial of an education programme for African-American and Latino attendees of STD clinics; Wang et al.[79] examined a randomised trial of sexually active adolescents in schools; and Heumann et al.[80] looked at an observational study of referrals provided to vulnerable uninfected adolescents for HIV prevention. All three found that the programmes under study were cost-saving for the healthcare system. Pinkerton et al.[81] found an intervention among African-American male adolescents to cost $57,327 per QALY when applied to all clients, but only $28,455 per QALY when restricted to those who were sexually-active at baseline. In a multi-centre study comparing a seven-session risk-reduction programme for those attending health-care facilities to a once-off education video, Pinkerton et al.[82] found the former to be cost-saving for male participants and to cost $32,688 per QALY for females.

4.1.3. General population interventions

Three articles considered population-based condom distribution schemes. In Louisiana Bedimo et al.[83] found such a programme to be cost-saving from a healthcare

perspective, based solely on the benefits gained by the state's African-American population. More broadly, Pinkerton et al.[84] estimated that a national distribution programme would be cost-saving, with or without making allowance for lost productivity costs averted. In the UK, Hughes and Morris[85] found that national condom distribution was extremely worthwhile for MSMs, costing £180 ($290) per LYG, but that coverage of heterosexuals was not cost-effective.

Papers by Holtgrave[86] and Holtgrave and Pinkerton[87] estimated the overall benefit of national prevention efforts and the probable benefits foregone if HIV incidence was not halved by 2005. When treatment costs were included, both papers found benefits far outweighed costs, although the form of future potential interventions was not specified. Gilson et al.[88] performed a randomised trial in 12 Tanzanian villages, setting up STD treatment facilities in half of them in order to reduce HIV transmissions both directly through better personal health and indirectly through education. The efficiency of the programme was estimated at around $10 per DALY saved. Rahman et al.[89] studied a national partner notification programme in Japan, estimating it at $4,930 per LYG, although this figure was extremely sensitive to willingness to identify sexual partners.

Two papers modelled the potential benefit of adding an HIV vaccine to WHO's Expanded Program of Immunization. In the first paper, which focused on Abidjan, Côte D'Ivoire, Cowley[90] found that a vaccine would be cost-saving from a societal viewpoint under a wide range of efficacy and seroprevalence assumptions. Bos and Postma's[91] later study, which looked at sub-Saharan Africa more generally, estimated a programme cost of just $3.4 per DALY saved.

4.1.4. Studies of multiple prevention interventions

Three papers compared the efficiency of a range of prevention interventions. Kahn and Sanstad[92] found both NEPs and risk behaviour education for gay community leaders to be extremely cost-effective, while screening surgeons for HIV infection was advisable. Over and Piot[93] estimated that well-focused condom distribution and blood screening programmes in a developing country setting would have cost-effectiveness ratios of ¢13 and ¢15 per DALY respectively. They also estimated that the case management of OIs, without the use of ART, would cost $235 to $384 per DALY saved. Hutton et al.[94] compared a broad range of prevention efforts in Chad. The most efficient interventions were peer-group education for sex workers and safer blood transfusion services, which cost less than $100 per case averted. An additional group of interventions – peer-group education for youth and high-risk men, and social marketing of condoms – were estimated to cost around $500 per case averted. Other programmes, including targeted and mass prevention programmes for pregnant women and voluntary HIV testing, had cost-effectiveness ratios ranging from $1,000 to $5,000 per case averted.

4.2. HIV Testing and Blood Screening

A total of 44 articles dealt with the cost-effectiveness of testing individuals for HIV or screening blood or blood products (table IV).[95-138] [*insert table IV around here*]

4.2.1. Testing pregnant women

Three articles considered the effect of VCT on pregnant mothers at a time when ART was not available. Brandeau et al.[95] found that the positive impact of testing in

California was mainly due to changes in risk behaviour induced in the mother, leading to the programme being potentially cost-saving. Houshayar[96] found that the seroprevalence of the population tested in New York was crucial, and that at a 1% HIV seroprevalence rate the programme cost $795 per infection detected. In France, Le Gales et al.[97] found that a universal screening programme might be cost-effective compared with no programme, but compared with a risk-factor based selective programme it had an ICER of around FF 400,000 ($68,860) per infection detected.

4.2.2. Testing patients and staff in hospitals

A review of a cohort study in St. Paul, Minnesota by Henry and Campbell[98] found that HIV testing, but not counselling, all inpatients in the hospital amounted to $12,700 per infection detected. Lurie et al.[99] modelled the impact of such a programme for the whole of the USA and found that while testing had a cost-effectiveness ratio of $16,104 per infected detected, the additional benefits for health care workers of such a programme were very slim. Owens et al.[100] conducted a study that included both patient and partner benefits of VCT in the US and found it to cost $55,000 per QALY saved. A study by La Croix and Russo,[101] which included benefits to patients, partners and healthcare workers, found a cost-benefit ratio of 1 to 239 in favour of VCT. Wilkinson et al.[102] looked at which type of test to use in Hlabisa, South Africa. They found that the use of one, or even two, rapid HIV tests cost less per post-test counselled individual than using the traditional enzyme-linked immunosorbent assay (ELISA), due to the far higher follow-up rate in this arm.

Mullins and Harrison[103] studied a cohort of trauma patients in Wichita, Kansas, but found universal testing not to be cost-effective due to the low seroprevalence among those using hospital services. Mathoulin-Pelissier et al.[104] modelled the effect of pre- or post-transfusion testing for transfusion recipients. They found pre-transfusion testing to cost $1,237 per infection detected, while adding post-transfusion testing raised this by a factor of seven. The use of a minimum benefit cut-off meant that some cheaper screening options were excluded from the final analysis.

Wallace and Carlin[105] considered testing newly diagnosed cervical cancer patients in London, UK, since HIV infection increases the risk of getting cervical cancer. The authors reported that if all patients were unaware of their serostatus this would cost more than £30,000 ($48,980) per HIV infection detected. Finally Mrus et al.[106] looked at the incremental benefit of testing by adding a fourth ELISA or a western blot (WB) to a 3-ELISA regime for testing infants born to seropositive mothers. Given the large proportion of true positives uncovered by the first three tests, the additional strategy had an ICER of $500,000 or more per infection detected.

Chavey et al.[107] considered annual HIV testing for all healthcare workers, as opposed to the use of universal precautions, and found the ICER to be in excess of $9 million per case averted. Owens et al.[108] estimated that a once-off testing of surgeons would cost almost $1.5 million per QALY saved and Sell et al.[109] reported similar results except in the case of dentists, which were estimated to cost around $139,000 per case averted. When Phillips et al.[110] included the impact of changing physician practice in the light of test results, cost-effectiveness ratios remained above $250,000 per case averted.

4.2.3. HIV testing at clinics

Varghese et al.[111] estimated that VCT in US clinics from a provider's perspective cost $31,943 per case averted, and that adding a partner notification arm had an ICER of $28,025 per case averted but were cost-saving from a societal perspective. Bos et al. conducted two studies of implementing routine HIV screening in STD clinics, first in Amsterdam[112] and then in Rotterdam.[113] In both cities the programme cost less than €3,000 ($3,390) per LYG, although the results were particularly sensitive to changes in sexual behaviour by seropositive clients. Farnham et al.[114] considered the benefit of VCT at STD, family planning and prenatal clinics. They reported that rapid testing reduced the cost per individual correctly informed of their serostatus, but only when results were provided prior to confirmatory tests.

Holtgrave et al.[115] considered the impact of all Counselling, Testing, Referral and Partner Notification (CTRPN) centres nationwide across the USA. They found that the benefit-to-cost ratio was more than 20 to 1, but as observed elsewhere[101], the results were very sensitive to a rise in risky behaviour among those who tested negative. Phillips and Fernyak[116] conducted a two-stage analysis of an expanded VCT programme, finding the programme to have a direct cost of $4,200 per infection detected, and estimated the additional benefit from getting patients onto triple-drug ART sooner rather than later at $23,300 per QALY saved. Finally Sweat et al.[117] used a randomised trial of VCT versus a video-based education intervention conducted among HIV clinic attendees in Nairobi and Dar-es-Salaam, Tanzania. The authors found that the programmes cost $13 and $18 per DALY respectively, without including treatment costs, and that targeting the programme, or getting couples to enrol together, improved these ratios.

4.2.4. Other testing interventions

The impact of pre-employment HIV testing in the USA was investigated by Bloom and Glied,[118] who found that for a large firm in a city with a relatively high seroprevalence rate such an approach might be cost-saving.

Zowall et al.[119] compared the cost to the Canadian public sector of testing immigrants for HIV prior to their arrival with the cost of treating infected migrants once in Canada. They found that the costs averted through pre-testing outweighed those incurred by between 1.5 and 5 times, although the study did not however include any potential benefits these immigrants might bring to Canada. Gorsky et al.[120] studied a cohort of recovering IDUs and estimated that a VCT programme would cost $341 per client per infected person detected; it would be cost-saving if one person in 260 avoided becoming infected through associated behaviour changes. Varghese and Peterman[121] modelled the effect of VCT on US prisoners due for release. The authors observed that at $33,953 per averted infection this would be cost-effective from a prison-system's perspective, and would be cost-saving once treatment costs were factored in. Blaxhaut et al.[122] evaluated the Swedish national VCT programme of the 1980s. They observed that specific programmes such as blood donor screening and prenatal testing had high cost-effectiveness ratios at $1.2 million and $96,000 per infection-detected, while testing outside national programmes and STD clinic screening had much lower ratios, at $26,000 and $18,000 per infection detected respectively.

4.2.5. Blood screening in high-income countries

Six studies dealt with the US blood screening programme, which used two ELISAs and a confirmatory WB as standard screening procedure. Eisenstaedt and Getzen[123] found this process to be cost-saving from a societal perspective, while Schwartz et al.[124] found a cost-effectiveness ratio of between $16,850 and $32,275 per infection detected, depending on the seroprevalence of donors. A secondary analysis in this last study estimated that using additional tests would cost at least $250,000 per additional case averted. Gelles[125] estimated a programme cost of between $36,300 and $128,833 per HIV–case averted, but that the cost per AIDS case averted was at least double these estimates. Adding an HIV-antigen test increased the cost to more than $12 million per case averted.

AuBuchon et al.[126] estimated that the existing screening programme in the USA cost $3,600 per QALY, but that adding a plasma p24 or an RNA polymerase chain reaction (PCR) test would cost more than $2 million per additional QALY saved. Jackson et al.[127] estimated that adding any form of nucleic acid testing to the existing regime would have an additional cost of $7-10 million per QALY, even when including benefits related to Hepatitis B and C. Busch et al.[128] used Hepatitis B seropositivity to predict HIV seropositivity. They estimated that this would cost just under $1 million per additional QALY saved, compared with existing procedures.

In France, Sailly et al.[129] estimated that a policy of using an ELISA and two confirmatory ELISAs would cost FF 676,596 ($116,480) per case averted. Djoussou et al.[130] focused on the incremental benefits of improving on this strategy, but none had an incremental cost below FF277 million ($47.7 million) per additional false-negative test avoided.

4.2.6. Blood screening in sub-Saharan Africa

Watson-Williams et al.[131] estimated that the reintroduction of blood screening in Uganda in 1988 cost ECU 21.5 ($24) per HIV negative unit produced. Laleman et al.[132] estimated that the cost-effectiveness of rapid testing from a programme perspective in Shaba, Zaire might be as low as ECU 137 ($155) per case averted. Foster and Buvé[133] found screening to be highly cost-effective at $1.3 per LYG in Monze, Zambia, even given that many clients were already seropositive. Benefits outweighed costs by a factor of three to one, after taking treatment costs into consideration. This result was confirmed by Jacobs and Mercer[134] in Mwanza, whose programme cost-effectiveness ratio was $2.7 per LYG and healthcare system cost-benefit ratio was one to 3.1. Finally, McFarland et al.[135] considered a programme to defer or test donors with high risk factors for HIV in a factory in Harare, Zimbabwe. Deferral, particularly if based on the presence of genital ulcers or STDs, including the cost of replacing deferred donors' donations, cost as little as $33 per case averted, while testing cost $100 per case averted.

4.2.7. Other blood-related interventions

AuBuchon and Birkmeyer[136] and Periera[137] both used observational studies data to model the effect of treating blood plasma in an industrialised setting. Considering solvent-detergent treatment and virus-inactivation respectively both articles found such processes not to be cost-effective with costs per QALY ranging from $300,000 to $700,000. Etchasson et al.[138] considered the benefits of preoperative autologous blood donation, but in no case was this cheaper than $235,000 per QALY, with much of the benefit arising from avoiding Hepatitis C treatment costs, rather those for HIV.

4.3. Prevention of Mother to Child Transmission

Thirty-one articles that dealt with the cost-effectiveness of preventing mother to child transmission using ART or other interventions (table V) were identified.[11, 139-168] [*insert table V around here*]

4.3.1. ART prophylaxis in high-income countries

Six of the nine studies conducted within the industrialized world – those by Gorsky et al.,[139] Grobman and Garcia,[140] Mauskopf et al.,[141] Lewis et al.,[142] Patrick et al.[143] and Postma et al.[144] – found that the use of ZDV was cost-saving when the cost of treating seropositive infants was included. Ecker[145] found a cost of $200,000 per case averted at the 1993 US national seroprevalence rate of 0.15% of the population, but that if the rate increased to 0.9% then routine VCT followed by ZDV treatment was cost-saving. Dunn et al.[146] did not consider treatment costs in their study, but their cost-effectiveness ratio of £35,000 ($57,150) per case averted was less than the lifetime treatment cost of a seropositive infant in the UK.[144] A study by Bramley et al.[11] considered the provision of dual therapy and caesarean section to all seropositive mothers in New Zealand. While the results, as in other studies, were sensitive to seroprevalence rates, the authors found the programme to cost $7,336 per LYG.

4.3.2. ART prophylaxis in sub-Saharan African countries

Five of the six MTCT studies in African settings focused on shortened ART regimes. The paper by Mansergh et al.[147] concluded that ZDV provision cost $3,148 per case averted from a healthcare perspective in an unspecified sub-Saharan setting. A

subsequent communication[148] updated earlier findings and reported a lower cost-effectiveness ratio, and that the intervention was cost-saving from a societal perspective. Marseille et al.[149] compared a range of long- and short-course ART combinations and found that the most efficient approach was targeted single dose nevirapine (NVP) for mother and child, with a cost-effectiveness ratio of $5.3 per DALY before infant treatment costs were considered.

Four other studies considered MTCT in South Africa. Wilkinson et al.[150] compared the provision of full-course ZDV with ZDV and lamivudine (3TC) and found dual therapy to be more cost-effective at $88 per LYG, without taking averted treatment costs into account. A subsequent analysis by the same authors[151] estimated that a short-course programme would cost ZAR 213 ($28) per DALY saved. Skordis and Nattrass[152] conducted a study of short-course regimes, allowing for non-ART treatment costs, and found single dose NVP provision to cost just $9.5 per DALY. Finally Wood et al.[153] estimated the cost of providing an unspecified prophylactic regime to cover between 25 and 75% of the seropositive pregnant women in South Africa to cost $19 per LYG. This increased to $133 per LYG when extended to the whole population.

4.3.3. Different ART prophylaxis regimes

In South Africa, Söderlund et al.[154] reported that treatment with intra- and post-partum ZDV to be both more expensive and less effective than treatment provided from the thirty-sixth week of pregnancy until birth. The incremental efficiency of switching to a full-length programme was over $4,000 per additional LYG. In the context of sub-Saharan Africa, Marseille et al.[155] modelled the progressive addition of post- and pre-

partum prophylaxis to an intrapartum regime, estimating incremental costs of $226 and $1,263 per DALY respectively. Pinkerton et al.[156] transferred results from the CDC-Thailand short-course trial[169] to a US setting to compare it with the long-course ZDV schedule of ACTG 076.[170] The authors estimated that the full-course regime cost a further $21,337 per additional case averted.

4.3.4. Other aspects of MTCT

Three studies considered mandatory screening versus voluntary testing of mothers or infants. In the US, Myers et al.[157] found that the additional cost of introducing mandatory compared with voluntary testing was almost $30,000 per case averted, while Immergluck et al.[158] estimated that mandatory testing was cost-saving in Chicago. The rate of adherence to prophylaxis by test recipients not captured through the voluntary programmes was a crucial determinant in these studies. Zaric et al.[159] studied the impact of enhanced voluntary maternal testing and routine newborn testing and found that implementing the practices jointly would have an additional cost of less than $11,000 per LYG.

Chen et al.[160] and Mrus et al.[161] considered adding elective caesarean section to a prophylactic regime in the USA; both studies found the procedure to be cost-saving. Halpern et al.[162] considered adding the procedure to other strategies. Adding elective caesareans to no ART appeared cost-saving, while adding it to ZDV or combination prophylaxis had an additional cost of less than $2,000 per LYG.

Stringer and Rose[163] studied whether to provide universal prophylaxis to all mothers or targeted prophylaxis to mothers who had had no antenatal care before delivery in the US.

Selective treatment was estimated to be cost-saving relative to no intervention, but that a shift to universal treatment would cost $350,000 per case averted. In Africa the same authors and colleagues[164] found targeted provision of NVP to cost $81 per case averted, increasing to $691 per case averted with universal provision. Rely et al.[165] considered various VCT and subsequent treatment options in Mexico. They found provision of zidovudine following targeted VCT, based on a risk questionnaire, to cost $39,220 per infection averted, and rapid testing of mothers arriving without antenatal care to be even more cost-effective.

Ratcliffe et al.[166] estimated the sequential benefits of adding various treatments to the UK healthcare system. Adding formula feeding to no treatment cost £15 ($24) per case averted, adding ZDV to this regime cost £7,658 ($12,500) per additional case averted and adding elective caesarean section as well as ZDV cost £27,836 ($45,450) per additional case averted. Two papers considered repeat maternal testing and partner testing for those women who initially tested negative. In the UK, Postma et al.[167] found partner testing was always cost-saving, while repeat testing provided benefits at a cost of £1,700 ($2,770) per LYG if used selectively, and £4,000 ($6,530) per LYG if universally applied. In a US setting, Sansom et al.[168] estimated that repeat testing cost $45,708 per LYG nationally, but was cost-saving among high-risk populations.

4.4. Anti-retroviral treatment

A total of 38 articles dealt with the cost-effectiveness of ART (table VI).[153,177-213]

[*Insert table VI around here*]

4.4.1. Zidovudine (ZDV) monotherapy

Three articles considered the cost-effectiveness of ZDV compared with no anti-retroviral therapy. Two focused on a small sample of individuals – Moore et al. [177] on a non-matched cohort, Messori et al.[178] on a clinical trial – and estimated a cost of between $34,000 and $37,000 per LYG respectively. McCarthy et al.[179] looked at providing ZDV to newly discovered asymptomatic patients following a national VCT programme. It estimated the cost of the programme to be less than $15,000 per LYG in high-risk populations such as IDUs and MSM, but to cost $1 million or more per LYG among lower risk groups.

4.4.2. Dual therapy

Six papers considered the cost-effectiveness of adding either 3TC or zalcitabine to ZDV. In three papers, Lacey et al.[180-2] used outcomes from the CAESAR trial, alongside cost data from individual countries. Using 'disease progressions avoided' as an outcome measure they found that over a one-year period adding 3TC was cost-saving in the USA, and cost less than $20,000 per disease progression averted in Canada, Germany and the UK. The short period of follow-up used in these studies has the benefit of reducing uncertainty as to the results presented, but excludes the impact of late-stage disease costs deferred through dual therapy.

Simpson et al.[183] developed a Markov model, based on broader outcomes data, in which zalcitabine was added to ZDV. The authors reported that across five European countries the cost-effectiveness ratio was relatively stable at between €12,000 ($13,550) and €21,000 ($23,710) per LYG. Chancellor et al.[184] modelled the same combination in the UK, finding a cost-effectiveness ratio of £6,276 ($10,250) per LYG. Davies et al.[185]

combined Chancellor et al.'s outcome model with observed costs at Adenbrookes hospital in Cambridge to find a cost of between £5,510 ($9,000) and £12,130 ($19,800) per LYG. Finally Mauskopf et al.[186] estimated the cost of adding 3TC to ZDV by modelling clinical trial data. Estimated costs varied from $14,000 to $27,000 per QALY, depending on the CD4 count at which treatment was commenced.

4.4.3. Triple therapy

Six studies compared triple therapy, or highly-active anti-retroviral treatment (HAART), with no ART. A US study by Freedberg et al.[187] found a cost of $23,000 per QALY while Sendi et al.,[188] estimated a ratio of CHF 33,000 ($24,530) per LYG. Two papers by Schackman et al.[189-90] observed that in the US starting HAART at a higher CD4 counts cost less than $20,000 per QALY gained, while in a third paper[191] the same authors reported that using community- or patient-based quality-of-life weightings did not significantly alter their findings. The paper by Wood et al. considering MTCT[153] also calculated that treating a quarter of those in need of HAART in South Africa would have a cost-effectiveness ratio of $15,000 per LYG.

A study by Moore and Bartlett[192] compared triple therapy to ZDV monotherapy, finding an incremental cost-effectiveness ratio of $10,000 per LYG. Cook et al.,[193] using clinical trial data which added indinavir to 3TC and ZDV therapy, concluded that over a five year time horizon this would be cost-saving, and over twenty years it would have an ICER of $13,229 per LYG. Miners et al.[194] considered adding an unspecified protease inhibitor (PI) to 3TC and ZDV in the UK and found an ICER of £17,698 ($29,340) per QALY, while Trueman et al.[195] modelled the addition of abacavir to 3TC and ZDV, and

found this to have an ICER of £16,168 ($26,400) per QALY when costs and benefits were discounted at similar rates. Anis et al.[196] used observational data from British Columbia, Canada to compare triple to dual drug therapies. They found the change in regime to cost between Can$ 46,971 ($33,510) and Can$ 58,806 ($41,960) per additional LYG.

4.4.4. Post-exposure prophylaxis (PEP)

Four studies focused on occupational PEP. Pinkerton et al.[197] estimated a ratio of $37,148 per QALY for triple therapy PEP, while Marin et al.[198] found a ratio of $190,392 per QALY across all needlestick injuries. When only injuries involving HIV seropositive individuals were considered, the cost was estimated to be around $50,000 per QALY. Li and Wong[199] found an average cost per case averted of $163,000 across a range of PEP therapies in the US. Finally King et al.[200] studied a small trial on the impact of using a rapid HIV assay to determine who should be given PEP. They found that the assay was cost-saving from a programme perspective because of its ability to reduce drug costs.

Lurie et al.[201], Pinkerton et al.[202-3] considered non-occupational PEP and results varied depending on the nature of the exposure. Those engaging in receptive anal sex or IDUs were most likely to be cost-effective, and were frequently cost-saving to treat, while those patients who repeatedly put themselves at risk of infection were the least efficient to treat.

4.4.5. Other ART-related issues

Ten studies covered additional ART-related topics. Wallace et al.[204] followed an open cohort of patients from 1995 to 1998, observing the fall in the death rate over time and estimating that costs rose by $17,500 per death averted, though the precise intervention was never specified. Boulle et al.[205] modelled a number of different HAART treatment approaches in South Africa. They estimated that using generic instead of patented drugs reduced the cost-effectiveness ratio by a third to ZAR 5,923 ($787) per LYG, and that adding a second line of therapy for 75% of those who failed their first line of therapy generated an ICER of ZAR 8,042 ($1,070) per LYG. Caro et al.[206] compared adding efavirenz or indinavir to ZDV and 3TC, and found that efavirenz-containing regimes were both cheaper and more effective than those including indinavir.

Tramarin et al.[207] compared hospital and home care and estimated that home-care patients cost the healthcare system less than hospital-care patients, even though the study did not include the cost of informal care. McCue et al.[208] studied the use of telemedicine for managing HIV-seropositive prisoners, and observed that the programme reduced the number of hospital visits made and cost less than the previous regime. Gibb et al.,[209] modelling the impact of prenatal testing in the UK in terms of the benefits to seropositive mothers from early detection and treatment with triple ART, estimated that the cost-effectiveness of this early diagnosis was around £50,000 ($81,640) per maternal LYG, too high to promote testing of mothers.

Allen et al.[210] investigated the use of recombinant human erythropoietin compared with the use of transfused erythropoietin in the treatment of ZDV-related anaemia in seropositive children and estimated an ICER of $1,373 per transfusion averted. Weinstein et al.[211] studied genotypic resistance testing, which was found to be cost-

effective generally for secondary resistance, with a cost ratio of under $20,000 per QALY, but only in populations with frequent drug-resistance for primary resistance. Goldie et al.[212] modelled hypothetical methodologies for raising adherence to ART, finding cheap interventions for late-stage disease patients to be most cost-effective. Johri et al.[213] evaluated the various AIDS Drugs Assistance Programs in the USA. They estimated that every increase in coverage of ART, or of OI prophylaxis, had an ICER of under $30,000, and concluded that even the most comprehensive package was cost-effective.

4.5. Prophylaxis and Treatment for Opportunistic Infections

A total of 27 articles were identified which dealt with either the prevention or treatment of HIV-related opportunistic infections (table VII).[214-240] [*insert table VII around here*]

4.5.1. OI Treatment

Freedberg et al.[214] considered a range of approaches for treating *Pneumocystis carinii* pneumonia (PCP). Among high and medium risk patients the most cost-effective strategies were to obtain a diagnosis through induced sputum analysis or assess the severity of the pneumonia by arterial blood gas analysis, respectively, before beginning treatment. Bennett et al.[215] compared trimetrexate and pentamidine as second line PCP treatments, and under rather stringent assumptions found trimetrexate at worst to cost $10 per additional percentage point rise in toxicity-free survival over a two week period. Wachter et al.[216] estimated that admitting patients with PCP to ICU cost $174,781 per LYG, based on an historical cohort covering the 1980s. Bennett et al.[217] compared liposomal doxorubicin with daunorubicin as treatment for Kaposi's sarcoma and reported

that the former cost $1,308 per additional patient responding to treatment compared with the latter. Finally Rachlis[218] compared intravenous to oral ganciclovir for CMV treatment, obtaining a cost-effectiveness ratio of $482 per progression-free day, which corresponded to $176,000 per progression-free year.

4.5.2. PCP prophylaxis

Castellano and Nettleman[219] and Freedberg et al[220] found that Trimethoprim-Sulfamethoxazole (TMP-SMX) was cost-effective compared with no prophylaxis, but that adding pentamidine was probably not. A third article, by Freedberg et al.,[221] found a TMP-SMX strategy to be both more expensive and less effective than treatment with dapsone, but that this result was extremely sensitive to relative drug efficacy and toxicity levels. The authors concluded that either drug might be cost-effective. Pentamidine had a very high ICER compared with dapsone. A fourth paper by Goldie et al.[222] modelled the impact of removing HAART patients from TMP-SMX prophylaxis once their CD4 counts had risen sufficiently. The study suggested that stopping at a count of 300 cells/mm^3 had an ICER of under $10,000 per QALY compared with stopping at 200 cells/mm^3. A secondary analysis in the same paper reported that the most cost-effective second line PCP prophylaxis combination was dapsone, followed by pentamidine and then atovaqone.

4.5.3. Mycobacterium Avian Complex (MAC) prophylaxis

Bayoumi and Redelmeier[223], Freedberg et al.[224] and Moore and Chaisson[225] studied MAC prophylaxis. The consensus indicated that azithromycin was the most cost-effective medication, followed by rifabutin, and that regimes including both these drugs

were more effective but at a considerable additional cost. Bayoumi and Redelmeier found an ICER of nearly $100,000 per extra QALY for adding azithromycin to a rifabutin regimen.[223] Sendi et al.[226] modelled the benefits of azithromycin for AIDS and non-AIDS patients. The benefits for AIDS patients were considerable at CHF 118 ($88) per LYG, but those for non-AIDS patients were not so great at CHF 60,000 ($44,600) per LYG. Scharfstein et al.[227] studied the optimal timing of starting azithromycin and concluded that beginning at a CD4 count of 50 cells/mm^3 is the most cost-effective policy, with an ICER of less than $30,000 per QALY.

4.5.4. Cytomegalavirus (CMV) prophylaxis

Moore and Chaisson[228], Paltiel and Freedberg[229] and Paltiel et al.[230] compared oral ganciclovir with no treatment, and found cost-effectiveness ratios of between $76,676 and $173,000 per QALY. Paltiel et al.[231] and Rose et al.[232] compared providing oral ganciclovir for all patients with only providing it to those with positive PCR tests for CMV disease. The studies found divergent results for the selective policy, $59,000 per QALY and $495,158 per LYG respectively, suggesting that even selective treatment may not be cost-effective.

4.5.5. Other OI prophylaxis

Scharfstein et al.[233] found fluconazole prophylaxis not to be cost-effective for preventing fungal infections, costing $96,000 per LYG even in endemic settings. Goldie et al. considered a range of screening strategies for cervical cancer in women[234] and anal squamous intraepithelial lesions in men.[235] The most cost-effective strategies were annual Papanicolau (Pap) screening for men and six-monthly Pap smears for women,

shifting to annual smears if the first two were negative. Finally Marra et al.[236] considered the administration of pneumococcal pneumonia vaccine and estimated that providing the vaccine directly through clinics was cost-saving, compared with no vaccine assistance or only prescribing it for clients. It should be borne in mind however that there is no conclusive clinical evidence of the benefit of this vaccine in general populations.[241]

Two papers considered tuberculosis (TB) prophylaxis for HIV positive individuals: Rose[237] in the USA and Bell et al. [238] in Uganda. In the USA six of the seven scenarios described were cost-saving if solely analysed in terms of direct TB-related costs, especially daily isoniazid for six months. In Uganda the various programmes are cost-saving only when lost productivity, patient costs and secondary case treatment costs were factored in, but the most cost-effective regime from a healthcare system perspective remained daily Isoniazid for six months at $114 per QALY.

Freedberg et al.[239] and Yazdanpanah et al.[240] modelled the impact of combinations of OI prophylaxis, and estimated that TMP-SMX, for PCP and toxoplasmosis, and azithromycin, for MAC, could be jointly provided at costs of less than $30,000 per additional QALY saved. Adding fluconazole for fungal infections had, in both cases, an ICER around $60,000 per QALY, and adding ganciclovir for CMV increased the cost per additional QALY gained to well over $100,000.

4.6. Mean Scores for the Studies in the Five Categories

The HIV Prevention studies (section 4.1) scored the highest, with a mean score of 25.0 (median 24; range 15 to 37), compared with a mean of 24.4 (median 26; range 11 to 32) for the Anti-Retroviral Therapy studies (section 4.4), a mean of 23.1 (median 22; range

19 to 28) for the Prevention of Mother to Child Transmission studies (section 4.3), a mean of 22.5 (median 22; range 14 to 34) for the HIV Testing and Blood Screening studies and a mean of 20.9 (median 24; range 19 to 31) for the Prophylaxis and Treatment of Opportunistic Infection studies (section 4.5).

The 95% confidence intervals for the Prophylaxis and Treatment for Opportunistic Infection studies were found to be below those of the HIV Prevention studies, the Anti-Retro-viral Therapy and the Prevention of Mother to Child Transmission studies (Figure 1). [*insert figure 1 around here*]

5. Discussion

This review had three objectives. First to provide health care professionals with a review of the cost-effectiveness literature published between 1994 and 2003. Second to highlight areas of work that urgently need to be performed, given the state of the HIV pandemic and contemporary containment programmes. Third to highlight some of the methodological issues raised by the studies performed to date and provide some recommendations for future studies.

Prevention of infection among adults through community interventions in high-risk, vulnerable groups appeared to be cost effective at a programme level both in high-income and sub-Saharan African countries; once lifetime treatment costs have been included it is often cost-saving. Possible exceptions to these results were observed among mentally ill adults and adolescents who were not yet sexually active. The level of risk behaviour of the population under consideration influences the cost-effectiveness ratio and studies considering general populations reported contradictory results.[83-85]

Testing healthcare workers routinely or cervical cancer patients after diagnosis did not appear to be cost-effective, while screening clinic attendees, particularly those attending STD clinics, appears to be cost-effective in both high and low income countries. Blood screening was reported to be reasonably cost-effective in high-income nations when carried out with an initial ELISA and two confirmatory tests, but additional tests or blood plasma treatment seemed to provide little extra benefit. Basic measures to improve blood services and initiate screening in sub-Saharan Africa were definitely cost-effective interventions, but no studies of the relative benefits of different test procedures in low-income settings were found.

MTCT was found to be cost-effective, if not cost-saving, across a broad range of settings, especially as elective caesareans sections have become commonplace in the industrialised world and short-course ART regimes are widely available in Africa. Longer treatment regimes in Africa and the imposition of mandatory testing in North America also appeared cost-effective.

HAART was reported to be incrementally cost-effective in high-income countries, at least up to triple therapy. Its use in sub-Saharan Africa is rapidly becoming more cost-effective as the price of HAART falls – the price of one common combination has fallen from $4,800 to $150 since December 2000.[242,243] This price reduction has greatly improved the cost-effectiveness of the use anti-retroviral therapy in middle- and lower income countries. Post-exposure prophylaxis appeared to be cost-effective for healthcare workers when the source of exposure was known to be seropositive, and for high-risk populations such as IDUs and MSM.

OI prophylaxis was found to be cost-effective for PCP, toxoplasmosis, and MAC. Fluconazole for fungal infections may be worthwhile, but ganciclovir for CMV had a high ICER, even when provided selectively. The OI treatment papers suggested that certain PCP treatment strategies are cost-effective, but that ICU admission was not in a pre-HAART cohort during the 1980s.

This review was limited as only studies published in English or French were considered. However only seven papers among the 1172 initially identified had been written in other languages. Furthermore, since only peer-reviewed published articles were considered, many of the studies that comprise the 'grey-literature' will have been missed by the search. This is even more likely to be the case for those studies that were conducted outside the USA or Western Europe, given that as little as 2% of Medline listed journals are published outside high-income nations.[244]

In considering the breadth of the literature, it is clear that some areas are very well dealt with, but others are not addressed at all. Among all the studies reviewed, only one dealt with HIV seropositive children,[210] and few considered adolescents[72,73,79,81] or infants.[90,91] Productivity losses, for employees or employers, were also rarely considered;[73,79,90,95,108,118,123,147,188] time and transport costs, which are often important when comparing hospital and community approaches to the same intervention, received minimal coverage.[67,68,80,81,82,111,238] Monitoring and evaluation of interventions was not considered in the studies reviewed, despite the potential costs that may be associated with this, especially in low-income settings, while empirical evidence of the cost-effectiveness of interventions to improve adherence to therapy was not included in any study.

Very few studies of community-based interventions have been published to date and those that have mainly focused on prevention efforts for vulnerable seronegative individuals in high-income countries. This needs to be redressed, in light of the likely future treatment and care of seropositive individuals in community settings. There were two exceptions: one study of STD treatment in Tanzania[88] and one on female sex workers in eastern and southern Africa.[69] Only one community-based HIV treatment study could be identified in this literature review,[207] but unfortunately its outcome measure would not allow for easy comparison with other hospital-based treatment interventions, nor did it include informal care costs. Although it has been suggested that community-based care, such as directly observed treatment (DOTS) may be cost-effective relative to hospital-based treatment or other forms of DOTS in the treatment of tuberculosis,[245] a debate exists concerning the applicability of such techniques in treating HIV infection.[246,247] Currently little published evidence exists on whether DOTS is cost-effective in the management of HIV-positive individuals.

Over 80% of studies reviewed focused on high-income countries, the majority of which were located in the USA. All papers dealing with low- or medium-income nations looked at sub-Saharan Africa, with the exception of one paper that covered the world[66] and another focusing on Mexico.[165] No published studies dealing with Asia, Latin America, and Eastern Europe could be identified, although a limited number of unpublished cost-effectiveness studies have been conducted in these regions.[248,249] This unbalanced pattern of research has previously been described.[250]

This lack of published evidence leaves health care professionals and policy makers less equipped to decide on the mix of interventions appropriate for their particular country.

The considerable differences in cost-effectiveness ratios found in high-income nations, relative to those reported from middle- or low-income countries are disconcerting. Furthermore, few studies have been published to date on the efficiency of tuberculosis treatment and care or the cost-effectiveness of ART in low-income countries.

The studies reviewed often failed to reflect the complexity of real-life situations. Some prevention papers assumed that the sexual interactions of their subjects were independent of each other when modelling the likelihood of disease transmission, even when considering a school-based population.[79] The two studies of the potential efficiency of an HIV vaccine did not consider how to dispense it, other than to infants – an important issue for non-infant, eligible populations when a vaccine first becomes available. In the field of MTCT, no study published by the end of 2003 considered the impact of triple-therapy, and nuanced considerations surrounding the lost productivity of HIV seronegative orphans have not been made.[30,35] Only one study studied the incremental benefit of second-line therapy,[205] but none had been published on the efficiency of third-line or salvage therapy by the end of 2003. Only one paper[206] compared the cost-effectiveness of different triple-therapy combinations; studies covering OIs did, however, often compare different drugs.

These gaps in the literature are disconcerting, since they indicate the limited evidence currently available for policy considerations. The methodological limitations associated with a number of the studies are also of concern, as they cast doubt on the results reported. Many of these limitations are due to a lack of original, context-specific information.[250]

Excluding the prevention literature, where the use of programme cost and behaviour change data was relatively common (see Table II), only a quarter of studies used original information as their primary data source. This presented a particular problem when the data was applied to a setting that differed either in time or location from that in which it was gathered, raising doubt as to the robustness of the findings.

A prime example can be seen in the MTCT literature. The ACTG 076 trial,[169] which was conducted in Western Europe and North America using ZDV prophylaxis, provided outcome data which were used by 14 different studies.[139,141-145,147,150,152,154,155,157,158,166] While more than half tried to adjust for differences in geographic settings, prophylaxis regime lengths or other factors, these studies often had to make considerable assumptions to fit the data to these differing contexts.

Over an eight-year period at least 20 studies on OIs and ART[186,189,190,192,193,206,211,213,221,222,227,228-235,239] used the same cost data source from 1991-2,[251] either as their primary cost and utilisation source or as part of a broader literature. Of these, only one study explicitly questioned whether such data were outdated,[213] while another verified their validity through other sources.[222] Changes in clinical practice and the relative costs of medical care over time may well have significantly affected costs, and therefore any efficiency estimates.[20] This implies not only that few studies collected their own data, but also that the conclusions presented in these studies are heavily dependent on the soundness of the original reference study.

Over time it is hoped that more local and contemporary data become available. As local trial data have become available the number of context-specific efficiency studies has

also increased. Two studies[186,221] tested whether a literature-based model produced similar results to one based on trial data and both reported that the two approaches provided similar cost-effectiveness results.

A common response to a lack of local or contemporary data is to model various scenarios using outcome and cost data from multiple, often unrelated sources. This is often seen in studies from sub-Saharan Africa,[147,150,152,154,155] but other authors have applied US health care costs to Thai outcomes data,[156], European costs to US trial data[183] or Canadian quality-of-life data to UK costs.[195] In many prevention studies, the number of HIV transmissions was modelled from observed changes in behaviour, using standardised, literature-based rates. The correlation between markers of behaviour change, such as self-reported reductions in sexual partners or use of shared needles, and HIV incidence may however differ widely between countries and regions, depending on cultural and other factors. Failure to account for such differences may significantly affect the results of the study.

The uncertainty introduced by such assumptions used in modelling exercises can to some extent be mitigated through the use of sensitivity analyses, providing insights on the robustness of the main findings. In this situation, most authors make conservative assumptions, assuming that if an intervention is cost-effective under these conditions then it will certainly be cost-effective under more realistic circumstances. This does however make comparisons between studies more difficult, since the magnitude of the biases introduced may be neither constant nor explicit. The problem was exacerbated by the use of widely varying outcomes measures.

Even when methodology was not problematic, several studies failed to present their work with clarity. An example of this was seen in the studies of OIs: in many of these papers it was impossible to know which drugs were being used, other than the specific intervention to treat the OI under observation.[214,215,217,218,224-226,237] This information is important since a study of managing CMV conducted in the era of HAART is not directly comparable with one conducted during the era of ZDV monotherapy. Few studies provided integrated or long-term analyses and only a very few studies analysed the use of a combination of interventions in a single setting,[239,240] or compared a range of interventions within a consistent analytical framework.[94,205,206,213]

The criteria, provided in Table I, were intended as a checklist to assess the methodological strength of the literature, rather than a scoring mechanism for comparing individual studies. As such it served a similar function as the criteria recently described for costing studies.[250] For instance, different analytic methods can arrive at different results, usually because they draw on different data. A Canadian cost-effectiveness study of HAART[252] published in 2004 and based on observational data for the period 1991-2001, estimated the additional cost per LYG to be $14,271 compared with an earlier modelling study which estimated the incremental cost to be between $33,510 and $41,960 depending on the comparator used.[196] However differences can also be observed within analytic methods. While some modelling exercises were based on empirical data derived from observational studies or randomized controlled trials, others used assumptions, which were primarily based on estimates.

It was notable that the mean scores and 95% confidence intervals for the Prophylaxis and Treatment of Opportunistic Infection section were significantly below those of three

other categories of study. This reflected the qualitative impressions and descriptions of these studies.

The literature on the efficiency of interventions in HIV infection can provide some clear policy implications for different types of intervention, but when more general conclusions are drawn, disagreements may arise.[3,253] A recent review comparing prevention with treatment and care interventions in sub-Saharan Africa[17] attempted to standardise outcomes post-hoc in order to determine which type of intervention was most efficient. As different types of interventions had different outcomes, the authors converted the results from these studies into a single CUA outcome measure.

The use of a single conversion rate for different populations in different geographic areas, however, failed to take account of the context-specificity of many of the interventions and their effects, though many of the conversions were not out of line with results reported in the general literature. Well-targeted HIV prevention efforts, especially when considered in isolation of each other, are often cost-effective if not cost-saving. Treatment and care interventions, however well focused, often have higher initial costs and, since the drugs currently being used cannot eliminate HIV infection, lower benefits.

Nevertheless, conclusions from such meta-analyses will only hold if the prevention efforts focus on vulnerable individuals, and if the cost of treatment and care remain constant over time and place. With the current rapid reductions in the price of ART[243,254] such assumptions may become rapidly outdated and broad policy statements, such as *"the next major increments of HIV funding in sub-Saharan Africa should be*

devoted mainly to prevention and to some non-HAART treatment and care"[253] seem to be based on a limited and static interpretation of the evidence.

The time and context-dependent nature of the results of many of these studies needs to be considered. For example, a study comparing ZDV monotherapy with no treatment may report that monotherapy is cost-effective, but once dual- or triple-therapies become available this conclusion will become outdated if the newer therapies prove more efficient. Similarly, while it may not have been cost-effective to manage people with PCP in ICU during the 1980s, this changed by the early 1990s due to changes in the baseline characteristics of patients who presented with PCP,[255] and by 2004 due to improved survival on HAART.

6. Conclusion

Research into the efficiency of HIV interventions has advanced significantly over the past decade, with the increase in data from trials and observational studies. Nevertheless, large gaps remain in both the data available[250] and the studies that have been performed.

As a consequence, too many studies have relied on data taken from multiple sources, rather than being able to use context specific and contemporary data. Many studies also provided poor descriptions of the actual interventions compared, data sources used and assumptions made, while the standards by which interventions are judged to be 'efficient' were not always transparent or consistent.

While the literature to date is able to guide policy in certain fields and for certain geographic locations, this is not the case for all settings. The paucity of the studies

coming from countries other than a few high-income nations is very disconcerting, and this will need to be addressed as part of monitoring and evaluating the scaling-up of treatment, care and prevention services in those countries with the greatest burden of disease. There is therefore an urgent need for a more systematic and rapid approach that seeks to answer policy-relevant questions as they emerge in this fast-developing and rapidly changing field.

One way to provide contemporary strategic information on the use, cost and outcome of HIV service provision is the development of multi-centre prospective monitoring systems. In addition to providing information to improve patient management and monitoring at health facility level, this can provide information to monitor and evaluate health care provision at health facility, sub-national and national levels.[256] Such information will be crucial for scaling up ART-related treatment and care in middle- and low income countries. However, despite the prevailing rhetoric on the 'need for evidence-based policy formulation and evaluation', the resources required to set up and maintain systems that could provide such strategic information often remain lacking.[257]

Table I. Review assessment criteria

	Criteria	Score[a] (maximum)		Criteria	Score (maximum)
1	Peer-reviewed article	1 (1)	9	Cost collection mechanism used:	
2	Model-based analysis	1		Multi-source	1
	RCT or Observational study	2 (2)		Single site	2
3	Total sample size:			Multiple sites	3 (3)
	Under 100	1	10	Cost data broken down	1 (1)
	Over 100	2 (2)	11	Cost and Utilisation data from Outcomes study	1 (1)
4	Co-morbidity controls used	1	12	Outcomes measures used:	
	Patients' age considered	1		Individuals seen	1
	Patients' gender considered	1		Cases detected	2
	Patients' ethnicity considered	1		LYG; Cases averted; QALYs; DALYs; CBA	3 (3)
	Other patient criteria considered	1 (5)	13	Timing of outcomes data collection:	
5	Cost perspective taken:			Retrospective	1
	Patient	1		Prospective	2 (2)
	Programme	2	14	Outcomes collection mechanism used:	
	Healthcare System	3		Multi-source	1
	Societal	4 (4)		Single site	2
6	Cost reference year provided	1 (1)		Multiple sites	3 (3)
7	Cost methodology used:		15	Empirical source of effectiveness data	1 (1)
	Variable costs only	1	16	Empirical source of quality of life weights	1 (1)
	Fixed and Variable costs	2 (2)	17	Nature of sensitivity analysis conducted:	
8	Nature of cost data used:			Univariate	1
	Estimates	1		Multivariate	2 (2)
	Charges	2	18	Statistical methods used	1 (1)
	Cost-adjusted charges	3	19	Confidence intervals used	1 (1)
	Actual costs	4 (4)	20	Discount rate used	1 (1)

a Each study could potentially score a maximum of 41 points. A score of 0 for a given question indicated either that the article did not consider the matter or that insufficient information was provided to allow a judgement to be reached. Question 16 was only relevant if the study was a cost-utility analysis.

Table II. Summary statistics of studies in the review

		Prevention	Screening & testing	MTCT	ART	OI Treatment	Total[a]
Total number of articles		36	44	31	34	27	176
Number including lifetime treatment costs[b]		26	25	26	22	15	114
Publication period	1987 to 1993	2	14	0	2	3	21
	1994 to 1996	5	14	6	3	2	30
	1997 to 1999	11	7	11	18	18	65
	2000 to 2003	18	9	14	15	4	60
National setting	USA	22	27	14	23	21	108
	European High Income	2	9	4	10	2	27
	Other High Income[c]	3	1	2	3	3	12
	Middle Income Africa	1	1	5	2	0	9
	Low Income Africa	6	6	5	0	1	18
	Other Low/Middle Income[d]	1	0	1	0	0	2
Intervention setting	Hospital or primary care	4	34	31	36	27	132
	Community[e]	26	5	0	0	0	31
	Both	6	2	0	1	0	9
	Other	0	3	0	1	0	4
Primary source of outcomes data	Observational study	8	16	2	7	1	34
	Randomised trial	11	1	0	8	2	22
	Published literature	17	27	29	23	24	120

a One article is included in both the MTCT and ART treatment sections of the review.[153] Its features are thus represented twice in this table.

b In prevention studies lifetime costs reflect costs from infection and are usually presented as a single figure; In treatment studies these costs generally reflect specific event costs as inputted into Markov models.

c Includes papers from Canada, Japan and New Zealand and articles covering more than one category.

d Includes a paper on Mexico and an article covering more than one category.

e Includes freestanding STD clinics.

Table III. Studies of interventions to prevent HIV infection among adolescents and adults

Authors	Location	Data source[a]; Setting	Population studied; Interventions used	Cost[b]: perspective; year; methodology; Lifetime treatment[c]	Measure of benefit	Interventions compared[d]	Outcome	Comment
4.1.1 Interventions to reduce unsafe injections								
Villari et al[59]	Italy	Literature; Community	Intravenous Drug Users; Annual Counselling, Testing and early Treatment	Healthcare System; 1991; Fixed and Variable; $ 36,288	Life Years Gained	Low (1%) seroprevalence	$ 1,040/LYG	Interventions were less efficient in higher seroprevalence populations
Holtgrave et al[60]	USA	Literature; Community	Intravenous Drug Users; Needle Exchange Programme & Pharmacy sales of sterile needles	Healthcare System; 1992; Fixed and Variable $ 108,469	Cases Averted (CA)	ACER at 100% coverage ICER of 80% vs. 70% coverage ICER of 100% vs. 90% coverage	$ 34,278/CA $ 68,557/CA $342,783/CA	Outcomes figures did not include lifetime treatment costs; Lifetime treatment cost quoted was 56% of referenced level due to low take-up of care by IDUs
Laufer[61]	New York state, USA	Survey, Literature; Community	Intravenous Drug Users; Needle Exchange Programmes	Healthcare System; 1996; Fixed and Variable; $ 195,188	Cases Averted	Programme perspective	$ 20,947/CA	The programme was cost-saving when lifetime treatment costs were included
Gold et al[62]	Hamilton, Canada	Literature; Community	Intravenous Drug Users; Needle Exchange Programme	Societal; 1995; Fixed and Variable; C$ 68,394	Cost-benefit ratio		1: 4.7	Cost and outcomes figures were conservative estimates; Lifetime cost used was 1991 figure, unadjusted for changes in prices or medical practice
Jacobs et al[63]	Edmonton, Canada	Observational study; Community	Intravenous Drug Users; Needle Exchange Programme	Programme; 1997; Fixed and Variable; -	Cases Averted		$ 9,537/CA	The study covered one year only – contacts remained at risk and future impact was not considered

[a] This refers largely to outcomes and direct cost data; indirect cost factors, lifetime HIV treatment costs, and other figures not directly observed in studies are generally taken from the relevant literature.
[b] When a study does not provide sufficient information for an assessment of a cost aspect to be made, or such an aspect is not considered, it is annotated '-'
[c] Lifetime cost figures refer to the cost of treating HIV over the full period of the disease. The net present value is provided if a discount rate is used in the source paper. Where annual or monthly figures are used, or a variety of figures are used by Markov model state, this is indicated.
[d] If no comparison is specified, the cost-effectiveness ratios are absolute.

Authors	Location	Data source[a]; Setting	Population studied; Interventions used	Cost[b]: perspective; year; methodology; Lifetime treatment[c]	Measure of benefit	Interventions compared[d]	Outcome	Comment
Zaric et al[64]	USA	Literature; Community	Intravenous Drug Users; Methadone Maintenance programme expansion	Healthcare System; 1998; Fixed and Variable; AIDS: $ 32,551 p.a. non-AIDS: $10,545 p.a.	QALY	High (40%) seroprevalence Low (5%) seroprevalence	$ 8,200/QALY $ 10,900/QALY	These results were robust, and suggested benefits to both IDUs and non-IDUs from such programmes
Laufer & Chiarello[65]	New York state, USA	Observational study; Hospital	Health Care Workers; Needlestick-prevention devices	Programme; 1992; Fixed and Variable; -	Injuries Averted (IA)	Injection equipment Recessed needles Needleless IV system vs. previous strategy	$ 984/IA $ 1,574/IA $ 790/IA	Outcomes included HBV-related injuries, which accounted for 51% of costs; The focus was on costs to the hospital as an employer
Dziekan et al[66]	10 of 14 worldwide sub-regions	Literature; Hospital	Health Care Workers and Patients; Providing single-use syringes and education	Programme; 2000; Fixed and Variable; -	DALYs	All high disease-burden sub-regions Worst subregion (Africa E) Best subregion (Europe B)	I$ 102/DALY I$ 14/DALY I$ 2,293/DALY	The cost-utility ratio for each subregion was never more than the average per capita income of that area
4.1.2 Interventions in other vulnerable populations								
Chesson et al[67]	New York Baltimore Seattle, USA	Randomised trial; Community	High risk urban women; Condom use and skills training sessions	Societal; 1996; Fixed and Variable; $ 195,000	QALYs	Programme perspective: Complete intervention Condom use section only Complete intervention vs. previous strategy	 $ 31,851/QALY $ 8,674/QALY $ 1,256,831/QALY	The condom use section was cost-saving when lifetime treatment costs and lost productivity were included
Holtgrave & Kelly[68]	USA	Randomised trial; Community	High Risk Urban Women; Skills training to increase Condom use	Societal; 1992; Fixed and Variable; $ 56,000	QALYs		$ 2,024/QALY	
Moses et al[69]	Nairobi, Kenya	Cohort study, Literature; Community	Female Sex Workers; Treating STDs, Increasing Condom Use	Programme; 1990; Fixed and Variable; -	Cases Averted	1% per act transmission rate; 50% condom use	$ 12/CA	Considered both primary infections of clients and secondary infections of clients' sexual contacts
Marseille et al[70]	Mpumalanga, South Africa	Literature; Community	Female Sex Workers; Female Condom distribution	Healthcare System; - Variable only; $ 2,507	Cases Averted	Programme perspective	$ 678/CA	The programme was cost-saving when lifetime treatment costs were included; Results were sensitive to the added protection of a female condom over a male one

Authors	Location	Data source[a]; Setting	Population studied; Interventions used	Cost[b]: perspective; year; methodology; Lifetime treatment[c]	Measure of benefit	Interventions compared[d]	Outcome	Comment
Pinkerton et al[71]	Biloxi, USA	Observational study; Community	Opinion leaders in the male gay community; Risk behaviour & communication education	Healthcare System; 1996; Fixed and Variable; $ 87, 045	Cases Averted; QALYs	Programme perspective	$ 65,458/CA	The programme was cost-saving when lifetime treatment costs were included
Kahn et al[72]	Eugene, OR & Santa Barbara, CA, USA	Observational study, Literature; Community	Young gay men; Risk behaviour education	Healthcare System; 2000; Fixed and Variable; $ 98,361	Cases Averted	Community based organisation perspective	$ 11,900/CA	Outcomes shown were those for stable seroprevalence; Rising seroprevalence improved the results slightly; All scenarios were cost-saving when lifetime treatment costs were included
						Holistic perspective (including expert advice)	$ 18,300/CA	
Tao & Remafedi[73]	Minnesota, USA	Observational study; Community	Gay and bisexual male adolescents; Personalised risk assessment, counselling and education	Societal; 1994; Fixed and Variable; $ 78,425	QALYs	Healthcare perspective	$ 6,180/QALY	Including lost productivity the programme had a cost-benefit ratio of 1: 9.65
Holtgrave & Kelly[74]	USA	Randomised trial; Community	Gay men with high risk behaviour; Risk behaviour education	Healthcare System; 1993; Fixed and Variable; $ 56,000	Cases Averted; QALYs	Programme perspective	$ 31,343/CA	The programme was cost-saving when lifetime treatment costs were included
Pinkerton et al[75]	Pittsburgh, USA	Randomised trial; Community	Male homosexuals; Safer-sex lecture and Skills training session	Healthcare System; 1992; Fixed and Variable; $ 56,000	Cases Averted; QALYs	Programme perspective: Lecture plus interactive skills session vs. lecture only	$ 4,150/CA	The programme was cost-saving when lifetime treatment costs were included
Johnson-Masotti et al[76]	USA	Randomised trial; Community	Adults with severe mental illness; One-on-one, group risk behaviour, or group advocacy sessions	Healthcare System; 1998; Fixed and Variable; $ 207,077	QALYs	One-on-one session	$ 26,305/QALY (M) cost-saving (F)	Gender-differentiated responses were significant
						Group behaviour sessions	$ 60,279/QALY (M) no QALY gain (F)	
						Group advocacy sessions	$ 41,980/QALY (M) $ 465,994/QALY (F)	
Pinkerton et al[77]	USA	Randomised trial; Community	Women with mental illness; Risk-reduction intervention	Healthcare System; 1999; Fixed and Variable; $ 214,707	QALYs	All participants	$ 136,295/QALY	Male trial participants did not change their behaviour at all
						Participants sexually active at time of intervention	$ 71,367/QALY	

Authors	Location	Data source[a]; Setting	Population studied; Interventions used	Cost[b]: perspective; year; methodology; Lifetime treatment[c]	Measure of benefit	Interventions compared[d]	Outcome	Comment
Sweat et al[78]	New York, USA	Randomised trial Community	African-American & Latino clients of STD clinics Video-based group intervention	Healthcare System; - Fixed and Variable; $ 199,990	Cases Averted; QALYs		$ 21,486/CA $ 1,613/QALY	The programme was cost-saving when lifetime treatment costs were included
Wang et al[79]	USA	Randomised trial, Literature; School	Sexually active adolescents; Risk-reduction intervention	Societal; 1994; Fixed and Variable; $ 148,518	Cost-benefit ratio		1: 2.65	The benefits included reduced antenatal and STD treatment costs; It was assumed that there was no overlap in the sexual activities among participants; Lost productivity figure used related to a 37 year old
Heumann et al[80]	San Francisco, USA	Observational study, Literature; Community	High risk seronegatives; Prevention referrals	Societal; 1999; Fixed and Variable; $ 130,000	Cases Averted	Programme perspective plus value of client's time	$ 20,738/CA	The programme was cost-saving when lifetime treatment costs were included
Pinkerton et al[81]	Philadelphia, USA	Randomised trial; Community	African-American Male Adolescents; Cognitive-behavioural risk-reduction intervention	Societal; 1997; Fixed and Variable; $ 195,188	Cases Averted; QALYs	All participants Participants sexually active at time of intervention	$ 57,327/QALY $ 28,455/QALY	The cost per CA was high in both scenarios, since an unusually large number of QALYs were saved by each case averted
Pinkerton et al[82]	Ten sites, USA	Randomised trial; Community	High risk attendees of health-care facilities; Cognitive-behavioural risk-reduction vs. video-based group intervention	Societal; 1999; Fixed and Variable; $ 214,707	QALYs	Male participants: cognitive-behavioural vs. video Female participants: cognitive-behavioural vs. video	Cost-saving $ 32,688/QALY	The video-based intervention was cost-saving compared to no intervention for all participants
4.1.3 General population interventions								
Bedimo et al[83]	Louisiana, USA	Observational study; Community	All African Americans in Louisiana; Condom Distribution	Healthcare System; 1996; Fixed and Variable; $ 195,188	Cases Averted; QALYs	Programme perspective	$ 17,652/CA	The programme was cost-saving when lifetime treatment costs were included; Ignores programme impact on non-African-Americans
Pinkerton et al[84]	USA	Literature; Community	National Population; Condom Distribution	Societal; 1996; Fixed and Variable; $195,188	Infections Averted		Cost-saving	Intervention remained cost-saving under all assumptions, even excluding lost productivity

Authors	Location	Data source[a]; Setting	Population studied; Interventions used	Cost[b]: perspective; year; methodology; Lifetime treatment[c]	Measure of benefit	Interventions compared[d]	Outcome	Comment
Hughes & Morris[85]	England and Wales, UK	Literature, Assumptions; Primary care	National Population; Condom provision by GPs	Healthcare System; 1993-4; Variable only; £ 51,200	Life Years Gained	Male Homosexuals Female Heterosexuals	£ 180/LYG £ 309,404/LYG	The cost per LYG for male heterosexuals was over £1.3m
Holtgrave[86]	USA	Literature, Assumptions; Community, Hospital	US population since 1985; Impact of existing HIV prevention efforts	Programme; 1978-2000; Fixed and Variable; $ 56,000-195,000	Cases Averted	Programme vs. worst-case alternative scenario Programme vs. best-case alternative scenario	$ 6,400/CA $ 49,700/CA	In all cases prevention efforts were cost-saving when treatment costs were included
Holtgrave & Pinkerton[87]	USA	Literature; Community, Hospital	US population until 2010; Impact of failing to reduce incident HIV infections	Programme; 2002-10; Fixed and Variable; $ 192,969	Cost benefit analysis		1: 49.2	No details on a methodology to reduce transmission were provided
Gilson et al[88]	Mwanza, Tanzania	Randomised trial; Community	12 villages in Mwanza; Improved STD treatment to reduce HIV infection	Programme; 1993; Fixed and Variable; -	DALYs	Tanzanian national life expectancy figures World Bank life expectancy figures	$ 10.33/DALY $ 9.45/DALY	This approach was almost as cost-effective as DOTS for tuberculosis
Rahman et al[89]	Japan	Literature; Hospital	Newly discovered HIV+ patients; Partner Notification	Healthcare System; 1997; Fixed and Variable; -	Life Years Gained		$ 4,930/LYG	Result was extremely sensitive to the level of co-operation from index cases in tracing contacts
Cowley[90]	Abidjan, Côte D'Ivoire	Literature/ Assumptions; Community	Children under age of 1; Hypothetical vaccine added to EPI schedule	Societal; 1988; Fixed and Variable; AIDS: $1,500 p.a.	Cost-benefit analysis	All scenarios	Cost-saving	A threshold analysis of a vaccine with 60% efficacy and 5% seroprevalence found a breakeven cost of $219 per dose from a healthcare system perspective
Bos & Postma[91]	Sub-Saharan Africa	Literature/ Assumptions; Community	Children under age of 1; Hypothetical vaccine added to EPI schedule	Programme; 1998; Fixed and Variable; -	DALYs	Assumed a vaccine efficacy of 60%	$ 3.4/DALY	Noted that all vaccines in trials were for HIV-1, subtypes B+ or E at the time of publication

Authors	Location	Data source[a]; Setting	Population studied; Interventions used	Cost[b]: perspective; year; methodology; Lifetime treatment[c]	Measure of benefit	Interventions compared[d]	Outcome	Comment
4.1.4 Studies of multiple prevention interventions								
Over & Piot[92]	Developing Countries	Literature; Community, Hospital	Various; Condom subsidisation, Blood Screening, AIDS management without ART	Healthcare System; - - -	DALYs	Condom distribution	$ 0.13/DALY	Focused on high risk individuals
						Blood screening	$ 0.15/DALY	When seroprevalence > 5%
						Case management of OIs	$ 235-384/DALY	Based on care provided through health clinics
Kahn & Sanstad[93]	USA	Literature; Community, Hospital	Various; Various	Programme; - Fixed and Variable; -	Cases Averted	Intravenous Drug Users (Needle Exchange)	$ 2,667/CA	Individual calculations were brief; Article focused on methodological issues
						Gay Community Leaders (Risk Behaviour Education)	$ 12,000/ CA	
						Surgeons (HIV Screening)	$ 194,186/CA	
Hutton et al[94]	Chad	Literature; Community, Hospital	Various; Wide range of prevention activities	Programme; 2002; Fixed and Variable; -	Cases Averted	Peer group education for:		A voluntary testing programme was estimated to cost $ 1,190 per CA; ZDV for pregnant women, treatment of STDs or breastfeeding advice cost between $939 and $ 2,748 per CA when targeted; Mass provision of these services was less CE
						Sex workers	$ 16/CA	
						Young people	$ 530/CA	
						High risk men	$ 580/CA	
						Safe blood transfusion	$ 84/CA	
						Condom social marketing	$ 534/CA	

Table IV. Studies of interventions to test patients or screen blood for HIV

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
4.21 Testing pregnant women								
Brandeau et al[95]	California, USA	Literature; Hospital	Pregnant Women; Counselling and Testing	Societal; 1988; - $ 50,620	Women screened	Effect on mothers and infants	$ 22-51/ woman screened	Savings were largely due to assumed changes in behaviour due to client serostatus knowledge; Lifetime treatment figure was net of seronegative care costs
						Effect on whole population	$ 152-cost-saving/ woman screened	
Houshayar[96]	New York, USA	Literature, Assumptions; Hospital	Pregnant Women; Counselling and Testing	Healthcare System; - - -	Infections Detected (ID)	1% seroprevalence	$ 795/ID	Considered a mixed population of high and low risk individuals; factored in likelihood of attending a screening programme
						0.1% seroprevalence	$ 6,870/ID	
Le Gales et al[97]	Paris, France	Cohort study; Hospital	Pregnant Women; Counselling and Testing	Healthcare System; 1987; Fixed and Variable; -	Infections Detected	Universal screening	FF 65,660-70,790/ID	Selective programme simulated from patient questionnaire
						Universal vs. selective screening by risk-factor	FF 393,020-424,510/ID	
4.2.2 Testing patients and staff in hospitals								
Henry & Campbell[98]	St. Paul, MN, USA	Cohort study; Hospital	Hospital inpatients; Testing only	Programme; - Fixed and Variable; -	Infections Detected	Hospital-specific perspective	$ 12,700/ID	When the national ELISA charge rate was used, the cost per ID rose to $15,402
Lurie[99]	USA	Literature, Expert consensus; Hospital	All Inpatients; Counselling and Testing	Healthcare System; - Fixed and Variable; $ 74,700	Infections Detected; HIV Cases Averted	Core analysis	$ 16,104/ID	Assumed a two year increase in length of ZDV treatment for seropositive clients, but no concomitant rise in life expectancy
						Healthcare Workers impact	$ 753 million/CA	
Owens et al[100]	USA	Literature; Hospital	All Inpatients; Voluntary Counselling and Testing	Healthcare System; 1993; Fixed and Variable; AIDS: $35,394 p.a., non-AIDS: $12,586 p.a.	QALYs	Benefit to patients and their sexual partners, 1% seroprevalence	$ 55,500/QALY	This programme cost $92,400/QALY when only benefits to screened patients were considered

[a] Lifetime cost figures refer to the cost of treating HIV/AIDS and related infections. The net present value is provided if a discount rate is used in the study.

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
La Croix & Russo[101]	USA	Literature; Hospital	All Patients; Counselling and Testing	Societal; - Fixed and Variable; -	Cost-benefit ratio	Benefits to healthcare workers, patient partners and patients, Seroprevalence of 3.67%	1: 239	Value of lost life, but not treatment costs, included; 100% serostatus ignorance assumed to maximise benefit; Very sensitive to rise in risky behaviour by seronegative clients
Wilkinson et al[102]	Hlabisa, South Africa	Cohort study; Hospital	Inpatients; Rapid and ELISA Testing	Programme; 1996; Variable; -	Post-test counselled individual (PTCI)	Cheapest single rapid test	R 14/PTCI	Rapid testing raised the counselling rate from 17 to 96% of clients by making a second visit unnecessary
						Double rapid test	R 45.2/PTCI	
						ELISA	R 83.8/PTCI	
Mullins & Harrison[103]	Wichita, Kansas, USA	Cohort study; Hospital	Trauma patients; Testing only	Programme; 1987-91; Fixed and Variable; -	Infections Detected	All identified cases	$ 24,300/ID	
						Serostatus unknown cases	$ 74,000/ID	
Mathoulin-Pelissier et al[104]	Bordeaux, France	Literature; Hospital	Blood transfusion recipients; 7 testing scenarios	Healthcare System; - - -	HCV or HIV Infections Detected	Pre-transfusion antibody test	$ 1,237/ID	Using a serum library and follow-up produced a lower cost-effectiveness ratio, but missed half the additional infections found by antibody testing
						Pre & post-transfusion antibody test	$ 8,322/ID	
Wallace & Carlin[105]	London, UK	Literature, Assumptions; Hospital	Women newly diagnosed with cervical cancer; Counselling and Testing	Programme; - Variable; -	Infections Detected	0.015% seroprevalence	£ 33,929/ID	All patients were assumed to be unaware of their serostatus
						0.85% seroprevalence	£ 588/ID	
Mrus et al[106]	USA	Literature; Hospital	Infants born to seropositive mothers; PCR and/or ELISA Testing	Programme; 2000; Fixed and Variable; -	Infections Detected	3 PCRs & an ELISA at 18 months vs. 3 PCRs[b]	$ 570,000/ID	The base case scenario captured a large majority of all cases, limiting the potential benefit of additional procedures
						4 PCRs (additional at 6 wks) vs. 3 PCRs	$ 720,000/ID	
Chavey et al[107]	USA	Literature; Hospital	Health Care Workers; Annual Testing	Programme; 1992; Fixed and Variable; -	Cases Averted	Annual testing vs. Universal precautions only	$ 9,177,615/CA	

[b] The three PCRs were carried out at 48 hours, one month and four months after birth. Where considered, a fourth PCR was carried out at six weeks post-partum.

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
Owens et al[108]	USA	Literature; Hospital	Surgeons; Testing at various frequencies	Societal; 1993; Fixed and Variable; $ 48,208	QALYs	One-off testing	$ 1,49 million/ QALY	Annual testing was more expensive and less effective than no testing from a societal perspective; Costs remained above $250,000/QALY when lost earnings were excluded
						Testing every 10 years	$ 3.87 million/ QALY	
Sell et al[109]	USA	Literature; Hospital	Surgeons and Dentists; Voluntary or Mandatory testing	Healthcare System; 1994; Fixed and Variable; $ 119,274	Cases Averted	One-off voluntary testing:		One-off mandatory programmes cost somewhat more per additional CA; Annual testing cost $1m per extra CA for dentists, and almost $20m for surgeons
						For Surgeons	$ 899,336/CA	
						For Dentists	$ 139,000/CA	
Phillips et al[110]	USA	Literature; Hospital	Physicians and Dentists; Voluntary or Mandatory testing	Societal; 1992; Fixed and Variable; $ 119,053	Cases Averted	Increased voluntary testing	$ 1.2 million/CA	The process was more cost-effective for dentists than for physicians; Prevalence and transmission risk strongly affected results
						Mandatory testing and inform patients	$ 395,000/CA	
						Mandatory testing and exclude from practice	$ 271,000/CA	
4.2.3 Testing clients at clinics								
Varghese et al[111]	USA	Literature; STD Clinic	All clinic attendees; Counselling, Testing and Partner Notification	Societal; 1997; Fixed and Variable; $ 175,000	Cases Averted	Provider costs for Counselling and Testing	$ 31,943/CA	All arms were cost-saving in societal terms, regardless of who carried out partner notification
						Partner Notification and Counselling and Testing vs. previous strategy	$ 28,025/CA	
Bos et al[112]	Amsterdam, Holland	Observational study, Literature; STD Clinic	All clinic attendees; HIV screening	Healthcare System; 2000; Fixed and Variable; € 59,000	Life Years Gained	Impact on primary infection cost and on secondary infections	€ 1,638/LYG	Results were sensitive to the level of behaviour change by those learning serostatus
Bos et al[113]	Rotterdam, Holland	Observational study, Literature; STD Clinic	All clinic attendees; HIV screening	Healthcare System; 2000; Fixed and Variable; € 59,000	Life Years Gained	Impact on primary infection cost and on secondary infections	€ 2,987/LYG	Intervention shown to be cost-effective in a low-prevalence setting; Results were sensitive to lifetime treatment costs

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
Farnham et al[114]	USA	Literature; Primary care, Clinic	STD & family planning clinics, prenatal clinic clients; Counselling and Testing	Programme/Societal; 1992; Fixed and Variable; -	Correctly informed individual (CII)	Seropositive individuals, rapid test Seropositive individuals, ELISA All participants, rapid testing All participants, ELISA	$ 940/CII $ 1,165/CII $ 37.31/CII $ 64.42/CII	All arms were compared to no treatment; Rapid tests yielded benefits only if results were provided on the same day – i.e. prior to confirmatory test results
Holtgrave et al[115]	USA	National database; Community	All CTRPN centre attendees; Counselling, Testing, Referral & Partner Notification	Societal; 1990; Fixed and Variable; $ 85,000	Cost-benefit ratio		1: 20.09	Results were sensitive to a rise in risky behaviour by those who discovered that they were seronegative
Phillips & Fernyak[116]	USA	Literature; Primary Care	All new clients; Expanded Counselling and Testing	Healthcare System; 1999; Variable; $ 231,000	Infections Detected; QALYS	Routine voluntary screening vs. current practice: Impact of testing only Additional impact of early treatment	$ 4,200/ID $ 23,300/QALY	A risk-factor based screening policy was less effective and more costly than the routine approach
Sweat et al[117]	Dar-es-Salaam, Tanzania & Nairobi, Kenya	Randomised trial; Community	HIV Clinic attendees; Voluntary Counselling and Testing	Programme; 1998; Fixed and Variable; -	Cases Averted; DALYs	Nairobi Dar-es-Salaam	$12.77/DALY $ 17.78/DALY	The programmes cost $249 and $346 per CA; Targeting efforts on high prevalence groups or enrolling couples jointly improved the results
4.2.4 Other testing interventions								
Bloom & Glied[118]	USA	Literature; Firm	Working adults; Pre-employment Testing	Societal, Employer; 1987; Fixed and Variable; $ 40-80,000	Cost-benefit analysis	Large firm with population seroprevalence of 0.14%	Cost-saving	Direct comparisons of costs and benefits were not made; A wide variety of results were offered
Zowall et al[119]	Canada	Literature; Hospital	Immigrants; Pre-migration Testing	Healthcare System; 1988; Fixed and Variable; $ 33,121-45,037	Cost-benefit analysis		1: 1.5-1:5	Only considered the cost of HIV testing and lifetime treatment

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
Gorsky et al[120]	USA	Cohort study; Methadone maintenance sites	Recovering IDUs; Counselling and Testing	Programme; 1991-2; Fixed and Variable; $ 56,000	Client	Client entering testing process	$ 215/Client	This programme would be cost-saving if 1 client in 260 avoided infection through changes in behaviour
						Client made aware of serostatus	$ 341/Client	
Varghese & Peterman[121]	USA	Literature; Prison	Soon-to-be-released inmates; Counselling and Testing	Healthcare and Prison system; 1999; Fixed and Variable; $ 186,900	Cases Averted	Prison system perspective	$ 33,953/CA	Used very little prison-specific data; The programme was cost-saving when lifetime treatment costs were included
Blaxhaut et al[122]	Sweden	National database; Hospital, Clinic	Blood donors, Pregnant women, STD clinic attendees, others; Counselling and/or Testing	Programme; 1991; - $ 140-280,000	Infections Detected	Blood Donor screening	$ 1.2 million/ID	The cost of all non-programme testing was $26,000 per ID; The costing methodology was sparse
						Prenatal testing	$ 96,000/ID	
						STD clinic screening	$ 18,000/ID	
4.2.5 Blood screening in high income countries								
Eisenstaedt & Getzen[123]	USA	Literature; Hospital	Blood Donors; Double ELISA and WB	Societal; 1986; Fixed and Variable $ 40,776	Life Years Gained; Cost-benefit ratio	Programme perspective	$ 10,885/LYG	
						Societal perspective	1: 1.2	
Schwartz et al[124]	USA	Literature; Hospital	Blood Donors; 7 HIV scenarios: base case Double ELISA and WB	Programme; 1988; Variable -	Infections Detected	0.029% seroprevalence, base case	$ 32,275/ID	All other options which were not dominated cost more than $250,000 per additional ID
						0.016% seroprevalence, base case	$ 16,850/ID	
Gelles[125]	USA	Literature; Hospital	Blood Donors; Double ELISA and WB, Plus HIV-AG in sensitivity	Healthcare System; 1989; Fixed and Variable; $ 12,908-25,816	Cases Averted	Cases of HIV averted	$ 36,300-128,833/CA	Also used a willingness-to-pay approach which valued each CA at a minimum of $1.6m; Briefly considered adding an HIV-AG test, finding it to cost of $12m-24m per additional CA
						Cases of AIDS averted (allowing for impact of primary illness)	$ 90,749-322,083/CA	

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
AuBuchon et al[126]	USA	Literature; Hospital	Blood Donors; Adding a plasma p24 or PCR to the existing antibody test	Healthcare System; 1995; Variable; AIDS: $37,000 p.a. non-AIDS: $7,400 p.a.	QALYs	Antibody testing	$ 3,600/QALY	The authors suggested that the PCR test may well be cost-effective in higher incidence settings
						Antibody and p24 antigen vs. previous strategy	$ 2.28 million/ QALY	
						Antibody and PCR vs. antibody testing only	$ 1.97 million /QALY	
Jackson et al[127]	USA	Literature; Hospital	Blood Donors; Adding Nucleic Acid Testing to existing procedures	Healthcare System; - - Stages 1&2: $15,000 p.a. Stages 3&4: $25,000 p.a.	QALY	Single donation NAT	$9.1 million/ QALY	Included HCV, HBV and HIV infection costs and benefits
						Minipool NAT	$ 7.1 million/ QALY	
Busch et al[128]	USA	Literature; Hospital	Blood Donors; HBV antibody testing	Healthcare System; 1995; Variable; AIDS: $37,000 p.a. non-AIDS: $7,400 p.a.	QALYs	Favourable assumptions	$ 992,000/QALY	Used HBV antibody positivity to detect patients during the window period of HIV infection
Sailly et al[129]	France	Literature; Hospital	Blood Donors; Current strategy: ELISA plus 2 confirmatory ELISAs	Programme; 1993; Fixed and Variable; -	Cases Averted	Current strategy	FF 676,596/CA	Also considered the efficiency of HBV, HCV and HTLV (leukaemia) testing
Djoussou et al[130]	France	Literature; Hospital	Blood Donors; 20 HIV testing scenarios, No counselling	Programme; 1996-7; Fixed and Variable; -	False Negatives Avoided	Best alternative vs. current strategy	FF 278 million/ FNA	The existing strategy was found to be the most efficient available

4.2.6 Blood screening in sub-Saharan Africa

Watson-Williams et al[131]	Uganda	Observational study; Hospital	Blood Donors; Introduction of blood screening	Programme; 1988-9; Fixed and Variable; -	HIV negative units produced		ECU 21.5/ HIV negative unit	
Laleman et al[132]	Shaba, Zaire	Observational study; Hospital	Blood Donors; HIVChek rapid assay	Programme; 1992; Variable; -	Cases Averted		ECU 179/CA	If unreported tests were used in a similar manner to those which were reported, then the programme would have cost ECU 137 per CA

Authors	Location	Data source; Setting	Population studied; Interventions used	Cost: perspective; year; methodology; Lifetime treatment[a]	Measure of benefit	Interventions compared	Outcome	Comment
Foster & Buvé[133]	Monze, Zambia	Observational study, Literature; Hospital	Blood Donors; HIVChek or ELISA, No counselling	Healthcare System; 1991; Variable; $ 110.60	Life Years Gained; Cost-benefit analysis	Programme perspective	$ 1.32/LYG	Took into account that many recipients were already seropositive; No provision was made for informing seropositive donors
						Healthcare system perspective	1: 3.0	
Jacobs & Mercer[134]	Mwanza, Tanzania	Observational study; Hospital	Blood Donors; Screening plus other measures to reduce likelihood of seropositive transfusion	Healthcare System; 1992; Fixed and Variable; $2,978-6,430	Life Years Gained; Cost-benefit analysis	Programme perspective	$ 2.7-2.8/LYG	Considered in isolation, the screening programme cost ¢20 per LYG; Lifetime treatment costs were converted from a 1988 study
						System perspective	1: 3.1-6.6	
McFarland et al[135]	Harare, Zimbabwe	Observational study, Literature; Factory	Blood Donors; Deferral on basis of risk factors and/or Testing	Programme; - Fixed and Variable; -	Cases Averted	Defer	$ 33-200/CA	Deferral (alone or combined with testing) was most efficient when genital ulcers or all STDs were used as risk factors
						Test	$ 100/CA	
						Defer and Test vs. previous strategy	Cost-saving - $ 1,578/CA	
4.2.7 Other blood-related interventions								
AuBuchon & Birkmeyer[136]	USA	Observational study, Literature; Hospital	Blood Plasma; Solvent-detergent treatment, No counselling	Healthcare System; - - Not specified	QALYs		$ 289,300/QALY	Hypothetical scenarios which dealt with particular patient groups gave costs per QALY ranging from $59,100 to $216,800
Pereira[137]	Barcelona, Spain	Observational study, Literature; Hospital	Blood Plasma; Virus-inactivation, No counselling	Healthcare System; 1997; - AIDS: $52,000 p.a. non-AIDS: $19,128 p.a.	QALYs		$ 2.16 million/ QALY	Cost-effective ratios remained over $700,000 per QALY, even when only high-risk scenarios were considered
Etchason et al[138]	USA	Literature; Hospital	Inpatients; Preoperative autologous donation	Healthcare System; 1992; Variable; $ 119,000	QALYs	Total Hip Replacement (most favourable procedure)	$ 235,000/QALY	HCV treatment costs included in the analysis composed the majority of total avoided treatment costs
						Prostatectomy (least favourable procedure)	$ 23.4 million/ QALY	

Table V. Studies of interventions to prevent HIV transmission from mother to child

Authors	Location	Population Studied; Interventions used[a];	Vertical transmission data source[b]; Maternal seroprevalence; External costs/benefits[c]	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
4.3.1 ART prophylaxis in high-income countries								
Gorsky et al[139]	USA	Pregnant women in prenatal care prior to third trimester; ZDV	ACTG 076; 0.17% -	Healthcare System; - Fixed and Variable $ 161,137	Cases Averted		Cost-saving	The intervention became cost-saving once the seroprevalence rate reached 0.11%
Grobman & Garcia[140]	USA	Pregnant women without prenatal care; ZDV & formula feeding	CDC-Thailand, Wade; 1.5% Additional costs of ZDV in sensitivity analysis	Healthcare System; 1997; Fixed and Variable; $ 169,642	Cases Averted	Base case Seroprevalence at 0.4%	Cost-saving $ 133/CA	
Mauskopf et al[141]	USA	Pregnant women in prenatal care prior to 34 weeks; ZDV	ACTG 076; 0.171% Additional costs of ZDV in sensitivity analysis	Healthcare System; 1994; Fixed and Variable; $ 98,915	Cases Averted		Cost-saving	
Lewis et al[142]	Memphis, USA	Specific cohort of pregnant women; ZDV	ACTG 076; 1.23% -	Healthcare System; - Fixed and Variable; $ 68,871 over 18 months	Cases Averted		Cost-saving	Despite having the data available, the study did not compare comprehensive voluntary testing to testing based on risk-factors only
Patrick et al[143]	British Columbia, Canada	Specific cohort of pregnant women; ZDV	ZDV; 0.037% Observational Study with ACTG 076-based regime; -	Healthcare System; - - C$ 220,708	Cases Averted; QALYs	Programme perspective	$ 2,200/QALY	Screening was significantly cost-saving when lifetime infant treatment costs were taken into account
Postma et al[144]	England, UK	Pregnant women in prenatal care; Formula feeding, caesarean & ZDV	ACTG 076, ECS; 0.01-0.15% 1 year of life gained from triple therapy	Healthcare System; 1995-6; - £ 178,300	Life Years Gained	All seropositives: 0.15% Status unaware seropositives: 0.01%	£ 3,300/LYG £ 114,000/LYG	The intervention was cost-saving when only the impact on the child was taken into account
Ecker[145]	USA	Pregnant women in prenatal care prior to 34 weeks; ZDV	ACTG 076; 0.15% 2 additional years of ZDV treatment costs	Healthcare System; 1993; Fixed and Variable; $ 123,819	Cases Averted		$ 198,509/CA	Sensitivity analysis suggested a more favourable result if seroprevalence was around 1.5%

[a] This refers to interventions over and above voluntary counselling and testing, which is provided in all interventions unless indicated otherwise.
[b] Source of effectiveness estimate for intervention. Unless otherwise specified source article's treatment regime is followed in the model.
[c] The consideration taken, if any, for increased maternal life expectancy or reduced adult-adult transmission due to early detection or treatment of HIV.

Authors	Location	Population Studied; Interventions used[a];	Vertical transmission data source[b]; Maternal seroprevalence; External costs/benefits[c]	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
Dunn et al[146]	London, UK	Pregnant women; ZDV	Assumptions; 0.176% -	Programme; - Variable; -	Cases Averted	Optimistic assumptions (75% reduction in transmission)	£ 35,000/CA	The worst-case scenario had a cost of £205,000 per CA; Treatment costs were not directly considered
Bramley et al[11]	New Zealand	Pregnant women; Universal VCT, dual therapy and caesarean	Meta-analysis; 0.03% 1 year additional cost and benefit	Healthcare System; 1999; Fixed and Variable; $ 68,868	Cases Averted; Life Years Gained		$ 267,944/CA $ 7,336/LYG	Results were sensitive to the HIV seroprevalence rate, which was estimated by expert opinion
4.3.2 ART prophylaxis in sub-Saharan Africa								
Mansergh et al[147]	Sub-Saharan Africa	Pregnant women; ZDV	Adjusted ACTG 076; 12.5% -	Societal; 1994; Fixed and Variable; $ 396	Cases Averted	Healthcare system perspective Societal perspective	$ 3,148/CA $ 1,115/CA	ZDV was provided for 2-6 weeks pre-partum and during labour; Continuing breastfeeding limited the benefits of intervention
Mansergh et al[148]	Sub-Saharan Africa	Pregnant women;	Adjusted CDC-Thailand; 12.5% -	Societal; 1997; Fixed and Variable; $ 432	Cases Averted	Healthcare system perspective	$ 1,269/CA	The intervention was cost-saving when productivity losses were included in the analysis
Marseille et al[149]	Kampala, Uganda	Various; ZDV, NVP or ZDV+3TC	HIVNET 012, PETRA, CDC-Thailand; 30% -	Healthcare System; 1999; Fixed and Variable; $ 281 (sensitivity analysis only)	Cases Averted; DALYs	Targeted, single dose NVP (HIVNET 012) Universal single dose NVP (HIVNET 012) Pre, intra & post-partum ZDV+3TC (PETRA-A) Intra- & post-partum ZDV+3TC (PETRA-B)	$ 5.25/DALY $ 11.29/DALY $ 105.31/DALY $ 47.92/DALY	A final arm using CDC-Thailand trial data (short-course ZDV treatment) cost $ 41.76 per DALY
Wilkinson et al[150]	Hlabisa, South Africa	Pregnant women in prenatal care; ZDV or ZDV+3TC	ACTG 076, Assumptions; 26% -	Healthcare System; 1997; Fixed and Variable; -	Life Years Gained	ACTG 076 regime with enhanced infrastructure ZDV+3TC with enhanced infrastructure	$ 198/LYG $ 88/LYG	Delivering the ACTG 076 regime through the existing infrastructure cost $ 205 per LYG compared to no treatment

Authors	Location	Population Studied; Interventions used[a];	Vertical transmission data source[b]; Maternal seroprevalence; External costs/benefits[c]	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
Wilkinson et al[151]	South Africa	Pregnant women; Short-course ZDV and formula feeding	CDC-Thailand, Assumptions; Nationally: 16% Provincially: 8.2-26.9% -	Healthcare System; 1997; Variable; -	Cases Averted; DALYs	National coverage within an enhanced health infrastructure	ZAR 213/DALY	Provincial cost-effectiveness ratios vary from ZAR 134-369/DALY; The highest incidence provinces were also the most cost-effective
Skordis & Nattrass[152]	South Africa	Pregnant women; ZDV or NVP	DITRAME, adjusted ACTG 076, HIVNET 012; 27% -	Healthcare System; 1999; - $ 1,621 (inpatient cost, no treatment costs)	Cases Averted; DALYs	Short course ZDV Single dose NVP	$ 25.1/DALY $ 9.5/DALY	The welfare cost of payments to the families of seropositive children was included as part of the total costs
Wood et al[153]	South Africa	Pregnant women; Unspecified prophylaxis	Meta-analysis; 12-16% (rising over time) -	Healthcare System; 2000; Variable; -	Life Years Gained	25% coverage 75% coverage 100% coverage	$ 19/LYG $ 19/LYG $ 133/LYG	Costs appeared to consist only of drug purchase costs; Did not specify which drugs were used
4.3.3 Different ART prophylaxis regimes								
Söderlund et al[154]	Soweto, South Africa	Pregnant women; ZDV, ZDV+3TC & formula feeding	ACTG 076, PETRA, CDC-Thailand; 15% -	Healthcare System; 1998 Fixed and Variable; Various	Life Years Gained	PETRA-B regime CDC-Thai regime vs. previous strategy ACTG 076 regime vs. previous strategy	$ 14/LYG Cost-saving $ 4,059/LYG	Adding free formula to the CDC-Thailand regime cost £ 910 per additional LYG; Study did not take adherence issues into account
Marseille et al[155]	Sub-Saharan Africa	Pregnant women; ZDV+3TC	Adjusted ACTG 076; 15% 30% adjustment for prevention benefits	Healthcare System; 1997; Fixed and Variable; $ 396	Cases Averted; DALYs	Intra-partum treatment Intra and post-partum vs. previous strategy Pre, intra and post vs. previous strategy	$ 60/DALY $ 226/DALY $ 1,263/DALY	The cost of drugs and tests, HIV prevalence, and treatment efficacy all had a significant impact on the cost-effectiveness ratios
Pinkerton et al[156]	USA	Seropositive pregnant women; Full and short-course ZDV	CDC-Thailand, ACTG 076; 100% -	Healthcare System; 1994; Variable; $ 88,635	Cases Averted	Short-course vs. full course ZDV	$ 21,337/CA	If the price of ZDV for the short-course programme was discounted by some 80%, to $50, the cost per additional CA rose to $ 27,010

Authors	Location	Population Studied; Interventions used[a];	Vertical transmission data source[b]; Maternal seroprevalence; External costs/benefits[c]	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
4.3.4 Other aspects of MTCT								
Myers et al[157]	USA	Pregnant women; ZDV	ACTG 076, Assumption; 0.17% 2 additional years of ZDV treatment costs	Healthcare System; 1995; Fixed and Variable; $ 100,000	Cases Averted	Mandatory vs. voluntary prenatal testing	$ 29,478/CA	Results were extremely sensitive to the level of ZDV adherence by mothers found to be seropositive
Immergluck et al[158]	Chicago, USA	Pregnant women; Full or post-partum ZDV	ACTG 076, Wade; 0.41% -	Healthcare System; 1997; Fixed and Variable; $ 171,374	Life Years Gained	Voluntary screening Universal screening vs. previous strategy	Cost-saving Cost-saving	At the Illinois seroprevalence rate of 0.15% universal screening cost $650 per LYG compared to no programme; At the national seroprevalence rate of 0.17% it cost $ 368 per LYG
Zaric et al[159]	USA	Pregnant women; Enhanced maternal or routine newborn screening	Meta-analysis; 0.17% Up to 4 years of life gained in sensitivity analysis	Healthcare System; 1997; Fixed and Variable; $ 143,000 (net of seronegative infant costs)	Life Years Gained	Enhanced voluntary maternal screening Routine newborn screening	$ 8,900/LYG $ 7,000/LYG	Implementing both strategies together cost $ 10,600 per LYG compared to the existing situation
Chen et al[160]	USA	Seropositive pregnant women; Elective Caesarean	Meta-analysis; 100% -	Healthcare System; 1998; Fixed and Variable; $ 86,130	Cases Averted		Cost-saving	All mothers had ZDV treatment throughout their pregnancy
Mrus et al[161]	USA	Seropositive pregnant women; Elective Caesarean vs. vaginal delivery	Meta-analysis; 100% -	Healthcare System; 1997; Fixed and Variable; $ 175,000	QALYs		Cost-saving	Although elective Caesarean had a lower cost and higher overall benefit it cause a slightly higher maternal mortality rate
Halpern et al[162]	USA	Seropositive pregnant women; Elective Caesarean vs. vaginal delivery	Meta-analysis; 100% -	Healthcare System; 1998; Fixed and Variable; $ 110,431	Cost Benefit Analysis; Life Years Gained	No ART ZDV prophylaxis Combination ART prophylaxis	1: 2.23 $ 17/LYG $ 1,697/LYG	
Stringer & Rouse[163]	USA	Pregnant women without prenatal care; Selective or universal emergency ZDV	Wade, Assumption; 5% -	Healthcare System; 1998; Fixed and Variable; $ 86,130	Cases Averted	Selective treatment Universal treatment vs. previous strategy	Cost-saving $ 342,068/CA	At national seroprevalence levels the selective treatment scenario cost $ 360,747 per CA

Authors	Location	Population Studied; Interventions used[a];	Vertical transmission data source[b]; Maternal seroprevalence; External costs/benefits[c]	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
Stringer et al[164]	Sub-Saharan Africa	Pregnant women; Maternal & infant NVP	HIVNET 012; 15% -	Healthcare System; 1999; Fixed and Variable; $ 281	Cases Averted	Study-eligible women: Targeted NVP	$ 81/CA	Treating the mother during labour and the infant once born cost $593 per additional CA; Among study-ineligible patients, treating only the infant was both cheaper and more effective than no therapy
						Universal NVP vs. previous strategy	$ 691/CA	
Sansom et al[165]	USA	Pregnant women initially testing HIV negative; ZDV, a protease inhibitor and ECS	PETRA, WITS, Literature; 0.017%, 0.62%; -	Healthcare System; 2000; Fixed and Variable; $194,250	Life Years Gained	National population (0.017% prevalence)	$45,708/LYG	The breakeven seroprevalence rate is 0.12%
						High-risk population (0.62% prevalence)	Cost-saving	
Ratcliffe et al[166]	UK	Seropositive pregnant women; Formula feeding, caesarean & ZDV	ACTG 076, ECS; 100% -	Healthcare System; 1996; Fixed and Variable; -	Cases Averted	Formula feeding	£ 15/CA	Adding ZDV to bottle feeding had an ICER of £ 9,186
						Formula & ZDV vs. previous strategy	£ 7,658/CA	
						All three interventions vs. previous strategy	£ 27,836/CA	
Postma et al[167]	London, UK	Initially seronegative pregnant women; Repeat or Partner Testing later in pregnancy	Literature, Assumption; 0.001-0.002% Reduced maternal seroconversion from partner testing	Healthcare System; 1995-6 Variable; Child: £178,300 Adult: £101,600	Life Years Gained	Universal repeat testing	£ 4,400/LYG	Results were very sensitive to the cost of the testing process; Partner testing, either universal or selective, was cost-saving across a broad range of sensitivity analyses
						Selective repeat testing	£ 1,700/LYG	
Rely et al[168]	Mexico	Pregnant women; ZDV or NVP after universal or targeted VCT	ACTG 076, HIVNET 012; 0.09%; 30% reduction in secondary adult transmission as sensitivity	Healthcare System; - Fixed and Variable; Child: $11,040 Adult: $ 31,848	Infant Infections Averted	85% VCT coverage, ZDV	$42,517/IIA	Incremental benefit of rapid HIV testing, and ZDV, for 60% of women arriving without prior VCT is $31,646/IIA over broad VCT; All NVP interventions have lower cost-effectiveness ratios
						VCT only if high-risk from questionnaire, ZDV	$39,220/IIA	

The transmission data sources used in table VI were: ACTG 076[169]; CDC-Thailand[170]; DITRAME[171]; ECS[172]; HIVNET 012[173]; PETRA[174]; Wade et al.[175] ; WITS[176]

Table VI. Studies of interventions to treat or prevent HIV using anti-retroviral drugs, and of related interventions

Authors	Location	Data source; Nature of analysis; Setting	Population studied; Interventions used;	Cost: perspective; year; methodology; lifetime treatment costs[d]	Measure of benefit	Interventions compared	Outcome	Comment
4.4.1 ZDV Monotherapy								
Moore et al[177]	Maryland, USA	Non-matched cohort; Decision model; Hospital	Seropositive patients; ZDV vs. no ART	Healthcare System; 1990; Fixed and Variable; Various	Life Years Gained		$ 34,600/LYG	Used full price Medicaid charge data
Messori et al[178]	USA	Randomised trial; Survival modelling; Hospital	Seropositive patients; ZDV vs. no ART	Healthcare System; 1996; Fixed and Variable; $93,125	Life Years Gained; QALYs		$ 36,890/LYG $ 47,112/QALY	The only cost difference between arms was drug cost
McCarthy et al[179]	USA	Literature; Markov model; Hospital	Seropositive patients; ZDV vs. no ART	Healthcare System; 1990; Fixed and Variable; $93,000	Life Years Gained	IDUs; MSM Male college students Female first time blood donors	$ 9,600/YLG $ 15,400/LYG $ 1.3m/LYG	Provided ZDV to serostatus-unaware, asymptomatic patients
4.4.2 Dual therapy								
Lacey et al[180] Lacey et al[181] Lacey et al[182]	CAESAR study	Randomised trial; No modelling performed; Hospital	Seropositive patients; Adding 3TC to ZDV or ZDV + didanosine/zalcitabine	Healthcare System; 1997; Fixed and Variable (USA, UK) Variable only (Canada, Germany); -	Diseases Progressions Avoided (DPA)	USA UK Germany Canada France Germany Italy Switzerland UK	Cost-saving £ 12,030/DPA DM 22,405/DPA C$ 14,225/DPA € 13,377/LYG € 17,916/LYG € 12,188/LYG € 15,129/LYG € 20,708/LYG	No follow-up beyond one year – savings were due to deferral of disease progression and costs Results were sensitive to the cost of hospital days and 3TC
Simpson et al[183]	Europe	Literature; Markov model; Hospital	Seropositive patients; ZDV + zalcitabine vs. ZDV	Healthcare System; 1992; Fixed and Variable; Various	Life Years Gained			US outcomes data and European nation costs were used

[d] In studies shown in tables VI and VII lifetime costs often varied depending on treatment strategy taken. For single intervention papers the treatment cost of the intervention arm is given. For multiple intervention papers a range covering the cost of all intervention arms is provided where possible. When lifetime costs are used, but no standardised figure provided, the term 'Various' is given.

Authors	Location	Data source; Nature of analysis; Setting	Population studied; Interventions used;	Cost: perspective; year; methodology; lifetime treatment costs[d]	Measure of benefit	Interventions compared	Outcome	Comment
Chancellor et al[184]	UK	Meta-analysis; Markov model; Hospital	Seropositive patients; ZDV + 3TC vs. ZDV	Healthcare System; 1995; Fixed and Variable; £ 50,551	Life Years Gained		£ 6,276/LYG	Lifetime treatment costs for ZDV monotherapy were modelled to be £44,612
Davies et al[185]	Cambridge, UK	Meta-analysis; Markov model; Hospital	Seropositive patients; ZDV + 3TC vs. ZDV	Healthcare System; 1998; Fixed and Variable; £ 4,590 p.a.	Life Years Gained		£5,510-£12,130/LYG	Used Chancellor et al.'s[179] progressions plus authors' own observed cost data
Mauskopf et al[186]		Randomised trial, Literature; Markov model; Hospital	Seropositive patients; ZDV + 3TC vs. ZDV	Healthcare System; 1995; Fixed and Variable; Various	Life Years Gained; QALYs	Modelling commencing at CD4 count >500 Trial population	$ 13,821/QALY $ 18,006/QALY	The least efficient outcome ($27,045 per QALY) was found when treatment began at a CD4 count of 100-199 cells/mm^3
4.4.3 Triple therapy								
Freedberg et al[187]	USA	Literature; Markov model; Hospital	Seropositive patients; HAART vs. no ART	Healthcare System; 1998; Fixed and Variable; $ 77,300	Life Years Gained; QALYs		$23,000/QALY	Lifetime treatment costs for ZDV monotherapy were modelled to be $45,460
Sendi et al[188]	Switzerland	Cohort study; Markov model; Hospital	Seropositive patients; HAART vs. no ART	Societal; 1997; Fixed and Variable; CHF 210,870	Life Years Gained	Healthcare system	CHF 33,000/LYG	The intervention was cost-saving when productivity losses were included
Schackman et al[189]	USA	Literature; Markov model; Hospital	Seropositive patients; ZDV + 3TC + efavirenz vs. no ART	Healthcare System; 1998, 1999; Fixed and Variable; $ 98,000 - $ 170,820 (depending on timing)	QALYs	Commencing at CD4 count of 500 vs. 200	$ 10,800/QALY	Commencing at CD4 count of 500 vs. no ART cost $17,300 per additional QALY saved
Schackman et al[190]						Commencing at CD4 count of 350 vs. 200	$7,000/QALY	Commencing at CD4 count of 350 vs. no ART cost $13,000 per additional QALY saved
Schackman et al[191]						500 vs. 200 using patient utility data 500 vs. 200 using community utility data	$ 18,400/QALY $ 20,100/WALY	The use of community or patient-base utility weights did not significantly affect the results
Wood et al[153]	South Africa	Literature; Decision model; Hospital	Seropositive patients; HAART vs. no ART	Programme; 2000; Variable only; -	Life Years Gained	25% population coverage	$ 15,000/LYG	

Authors	Location	Data source; Nature of analysis; Setting	Population studied; Interventions used;	Cost: perspective; year; methodology; lifetime treatment costs[d]	Measure of benefit	Interventions compared	Outcome	Comment
Moore & Bartlett[192]	USA	Literature, Assumptions; Decision model; Hospital	Seropositive patients; ZDV + 3TC + IDV vs. ZDV	Healthcare System; 1992; Fixed and Variable; Various	Life Years Gained		$10,000/LYG	If triple therapy cost the same as ZDV then the cost was $18,000 per additional LYG
Cook et al[193]	USA	Randomised trial; Markov model; Hospital	Seropositive patients; ZDV + 3TC + IDV vs. ZDV +3TC	Healthcare System; 1996; Fixed and Variable; $ 70,655 over 5 years	Life Years Gained	20 year projection	$ 13,229/LYG	This intervention was cost-saving over a five year time horizon
Miners et al[194]	UK	Observational study; Markov model; Hospital	Seropositive patients; Adding a PI to dual therapy	Healthcare System; 1999-2000; Fixed and Variable; £ 119,190	Life Years Gained; QALYs		£ 14,602/LYG £ 17,698/QALY	Results were sensitive to the discount rate
Trueman et al[195]	UK	Observational study; Markov model; Hospital	Seropositive patients; ZDV + 3TC + ABC vs. ZDV + 3TC	Healthcare System; 1997; Fixed and Variable; £ 87,965	Life Years Gained; QALYs		£ 8,149/LYG £ 10,254/QALY	When QALYs were discounted at the same rate as costs, the intervention cost £16,168 per additional QALY saved
Anis et al.[196]	British Columbia, Canada	Observational study; Decision analysis; Hospital	Seropositive patients; HAART vs. various dual therapies	Healthcare System; 1997; Fixed and Variable; Various	Life Years Gained	Triple therapy vs. ZDV-based dual therapy Triple therapy vs. d4T-based dual therapy	$Can 58,806 $Can 46,971	The difference in LYG between the two dual-therapies was negligible, but the d4T arm cost more
4.4.4 Post-exposure prophylaxis								
Pinkerton et al[197]	USA	Literature; Decision model; Hospital	Healthcare workers; ZDV+3TC+IDV prophylaxis	Healthcare System; 1996; Fixed and Variable; $ 98,000	QALYs	0.3% seroconversion risk	$ 37,148/QALY	The effectiveness of the intervention was assumed; Results were sensitive to the effectiveness and cost of prophylaxis
Marin et al[198]	USA	Literature; Decision model; Hospital	Healthcare workers; ZDV or ZDV+ 3TC+INV prophylaxis	Healthcare System; 1996; Variable; $ 195,000	QALYs	ZDV monotherapy Triple therapy	$ 175,222/ QALY $ 190,392/ QALY	If all exposed blood came from seropositive patients then ZDV prophylaxis cost $50,041 per QALY
Li and Wong[199]	USA	Literature; Decision model; Hospital	Health Care Workers; ZDV, ZDV+3TC, or ZDV+3TC+IDV prophylaxis	Programme; - Variable; -	Cases Averted	0.32% seroconversion risk	$ 163,000/CA	Model is very basic, performed over half a page in a letter to the editor

Authors	Location	Data source; Nature of analysis; Setting	Population studied; Interventions used;	Cost: perspective; year; methodology; lifetime treatment costs[d]	Measure of benefit	Interventions compared	Outcome	Comment
King et al[200]	St Gallen, Switzerland	Randomised trial; No modelling performed; Hospital	Healthcare workers; Rapid assay to determine prophylaxis recipients	Programme; 1998-9; Variable; -	Cases Treated		Cost-saving	Study focused largely on psychological outcomes
Lurie et al[201]	USA	Literature, Assumptions; Decision model; Hospital	Non-occupational HIV exposed individuals; ZDV+3TC	Programme; - Fixed and Variable; -	Cases Averted	Assume 80% PEP effectiveness and 1% seroconversion risk	$ 136,500/CA	The outcome was sensitive to the drug regime provided and whether the source of exposure was known to be seropositive
Pinkerton et al[202]	USA	Literature, Assumptions; Decision Model; Hospital	Sexually HIV exposed individuals; ZDV, ZDV+3TC or ZDV+3TC+IDV	Healthcare System; - Fixed and Variable; $ 195,188	QALYs	Receptive anal intercourse, 18% chance partner is seropositive	$ 6,354/QALY	Other scenarios all had cost-utility ratios over $750,000 per QALY
Pinkerton et al[203]	USA	Literature; Decision model; Hospital	Non-occupational HIV exposed individuals; ZDV+3TC+ a PI	Healthcare System; - Variable; $ 195,000	QALYs	Receptive anal intercourse, partner known seropositive Intravenous Drug User, 50% chance partner is seropositive	Cost saving $ 12,751/QALY	Simplified model; In lower risk scenarios CE ratios are over $1m/QALY
4.4.5 Other ART-related issues								
Wallace et al[204]	San Diego, USA	Open historic cohort; No modelling performed; Hospital	Seropositive patients; Various triple therapy combinations	Patient; 1995-8; Fixed and Variable; -	Deaths Averted (DA)		$ 17,500/DA	The study population did not seem comparable over time; All patients received MAC and PCP prophylaxis
Boulle et al[205]	South Africa	Literature; Decision modelling of 8 scenarios; Hospital	Seropositive patients; Specific ranges of triple therapies	Healthcare System; - Fixed and Variable; -	Life Years Gained	Generic drugs Patented drugs	ZAR 5,923/LYG ZAR 9,089/LYG	The choice of drugs was dictated by cost considerations
Caro et al[206]	USA	Literature; Decision model; Hospital	Seropositive patients; Efavirenz vs. indinavir combined with 2 NRTIs	Healthcare System; 1998; Fixed and Variable; Various	Life Years Gained		Cost-saving	Efavirenz-containing regimes were always cheaper and more effective than indinavir-containing ones
Tramarin et al[207]	Vicenza, Italy	Randomised trial; No modelling performed; Hospital, Community	AIDS patients; Home vs. hospital care	Healthcare System; 1990; Fixed and Variable; $10,505 – $ 27,764	Well weeks	Home care patients Hospital care patients	$ 482/WW $ 791/WW	Did not include the cost of informal care by relatives; No incremental analysis performed

Authors	Location	Data source; Nature of analysis; Setting	Population studied; Interventions used;	Cost: perspective; year; methodology; lifetime treatment costs[d]	Measure of benefit	Interventions compared	Outcome	Comment
McCue et al[208]	Virginia, USA	Observational study; No modelling performed; Prison	Seropositive prisoners; Telemedicine	Healthcare System; 1995-6; Fixed and Variable; -	Visits		$ 241 saved/ Visit	Did not consider any potential difference in benefit between a telemedicine consult and a clinic visit
Gibb et al[209]	UK	Literature; Markov model; Hospital	Pregnant women; ART triple therapy after antenatal testing	Healthcare System; 1996-7; Fixed and Variable; £ 102,881	Life Years Gained	Benefit to mother of early diagnosis (An average of 20.4 months)	£ 51,258/LYG	Prenatal testing did not appear to be cost-effective if only maternal benefits were considered; Beginning ART at diagnosis or at a 350 CD4 count had little impact
Allen et al[210]	Ottawa, Canada	Literature; Decision model; Hospital	Seropositive children; Recombinant Human Erythropoietin or Transfusions for ZDV-related anaemia	Healthcare System; 1994; Fixed and Variable; -	Transfusions Averted		$ 1,373/TA	The study did not provide outcomes measures which were comparable with the rest of the literature
Weinstein et al[211]	USA	Literature; Markov model; Hospital	Seropositive patients; Genotypic resistance testing for patients with drug resistance	Healthcare System; 1998; Fixed and Variable; $ 90,650 - $97,790 (post-failure lifetime)	QALYs	CPCRA 046 efficacy data	$ 17,900/QALY	In settings with frequent drug resistance in naïve patients (>4%) initial testing was also cost-effective
						VIRADAPT efficacy data	$ 16,300/QALY	
Goldie et al[212]	USA	Assumptions; Markov model; Community	Seropositive patients on antiretrovirals; Counselling, Beepers, Automatic dispensing systems & DOT	Healthcare System; 2001; Fixed and Variable; Various	QALYs	$100/month intervention, 10% improvement, late disease patients	$ 31,000/QALY	Incremental CE ratios range from $22,400 to $242,100 per QALY; All effectiveness data is hypothetical
Johri et al[213]	USA	Literature; Markov model; Hospital	Patients in 11 ADAP programmes; Various combinations of HAART and OI prophylaxis	Healthcare System; 1999; Fixed and Variable; $ 77,800 - $ 149,000	QALYs	Most comprehensive coverage scenario vs. next least comprehensive non-dominated scenario	$ 25,000-28,000/QALY	The cost-utility ratio of adding new services never rose above $30,000 per QALY

Table VII. Studies of interventions to treat or prevent opportunistic infections

Authors	Location	OI studied; Other drugs provided	Intervention used; Nature of Analysis	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
4.5.1 OI Treatment								
Freedberg et al[214]	USA	*Pneumocystis Carinii* Pneumonia; -	Initial testing or empiric antibiotics; Decision model	Healthcare System; 1989; Fixed and Variable; -	QALYs	High risk patients: induced sputum analysis Intermediate risk: arterial blood gas analysis Low risk: 7 days of Erythromycin	$ 34,174/QALY $ 4,593-8,310/QALY $ 675-3,306/QALY	In each risk group the strategy chosen by the authors was that which provided the longest projected life expectancy at an ICER of less than $50,000 per QALY
Bennett et al[215]	USA	*Pneumocystis Carinii* Pneumonia; -	Trimetrexate vs. Pentamidine after TMP-SMX failure; Decision model	Programme: - Fixed and Variable; -	Toxicity Free Survival (TFS)	Similar efficacy assumed	$ 10 per 1% increase in TFS	Efficacy levels were assumed throughout the study
Wachter et al[216]	USA	*Pneumocystis Carinii* Pneumonia; None	Admission vs. Non-admission to ICU; Historical cohort study	Healthcare System; 1991; Fixed and Variable; -	Life Years Gained	Average over whole period	$ 174,781/LYG	Period-specific outcomes were: 1981-85: $305,795/LYG 1986-88: $94,528/LYG 1989-91: $215,233/LYG
Bennett et al[217]	USA	Kaposi's sarcoma; -	Doxorubicin vs. Daunorubicin; Decision model	Programme; - Variable only; -	Responder		$ 1,308/Responder	A responder was a patient whose condition improved after treatment
Rachlis[218]	Canada & USA	Cytomegalovirus; -	Intravenous vs. oral Ganciclovir; Non-blind randomised trial	Societal; 1993-5; Fixed and Variable; -	Progression Free Survival		$ 482/ Progression Free Day	From a public healthcare system perspective the intervention cost $409 per progression free day
4.5.2 PCP Prophylaxis								
Castellano & Nettleman[219]	USA	*Pneumocystis Carinii* Pneumonia; ZDV	Pentamidine or TMP-SMX; Markov model	Programme; - Fixed and Variable; Various	Life Years Gained	TMP-SMX Pentamidine	$ 23,711/LYG $ 21,461/LYG	TMP-SMX was both cheaper and more effective than pentamidine
Freedberg et al[220]	USA	*Pneumocystis Carinii* Pneumonia; ZDV	Pentamidine, TMP-SMX, or Dapsone; Markov model	Healthcare System; 1989 Fixed and Variable; -	Life Years Gained	Dapsone Pentamidine vs. dapsone	$ 13,400/LYG $ 756,000/LYG	Dapsone was both cheaper and more effective than TMP-SMX, although the result was sensitive to relative drug efficacy and toxicity

Authors	Location	OI studied; Other drugs provided	Intervention used; Nature of Analysis	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
Freedberg et al[221]	USA	*Pneumocystis Carinii* Pneumonia; ZDV	Pentamidine or TMP-SMX; Markov model comparing literature and RCT data	Healthcare System; 1991-2; Fixed and Variable; -	Life Years Gained	Literature-based model: TMP-SMX	$ 350/LYG	Pentamidine cost $110,880 per additional LYG compared to TMP-SMX in the literature-base model
						RCT-based model: TMP-SMX	$ 720/LYG	
Goldie et al[222]	USA	*Pneumocystis Carinii* Pneumonia; HAART with TMP-MSX and Azithromycin	Removing patients from TMP-SMX at CD4 counts of 200 or 300; Markov model	Healthcare System; 1999; Fixed and Variable; $ 144,260 - $146,310 (depending on strategy)	QALYs	Stopping at 200 CD4 count	$ 5,100/QALY	An analysis of second line prophylaxis strategies found dapsone, pentamidine, atovaquone to be the most efficient combination at $4,500 per QALY
						Stopping at 300 CD4 count	$ 9,400/QALY	
4.5.3 MAC Prophylaxis								
Bayoumi & Redelmeier[223]	North America	Mycobacterium avium complex; HAART with a PI	Azithromycin, rifabutin or clarithromycin; Markov model	Healthcare System; 1997; Fixed and Variable; $ 233,000	Life Years Gained; QALYs	Rifabutin	$ 41,500/QALY	Clarithromycin was more expensive and less effective than azithromycin
						Azithromycin vs. Rifabutin	$ 54,300/QALY	
						Azithromycin & Rifabutin vs. Rifabutin	$ 96,300/QALY	
Freedberg et al[224]	USA	Mycobacterium avium complex; -	Azithromycin rifabutin, or clarithromycin; Decision model	Programme; 1994; Fixed and Variable; Various	QALYs	Rifabutin	$ 179,100/QALY	Results were most sensitive to the cost of prophylaxis, the survival impact of treatment and initial CD4 counts
						Azithromycin	$ 58,200/QALY	
						Clarithromycin	$ 116,900/QALY	
Moore & Chaisson[225]	USA	Mycobacterium avium complex; -	Azithromycin, rifabutin, or clarithromycin; Decision model	Programme; 1996; Fixed and Variable; -	MAC Cases Averted (over 12 months)	Azithromycin	$ 24,097/MAC CA	Rifabutin prophylaxis was more expensive and less effective than other therapies
						Clarithromycin	$ 25,482/MAC CA	
						Rifabutin & Azithromycin	$ 26,527/MAC CA	
Sendi et al[226]	Switzerland	Mycobacterium avium complex; HAART	Azithromycin; Markov model	Healthcare System; 1997; Fixed and Variable; Yes	Life Years Gained	Patients without AIDS	CHF 60,000/LYG	All patients were assumed to receive HAART and TMP-SMX (HAART was assumed to be effective for 3 years)
						Patients with AIDS	CHF 118/LYG	

Authors	Location	OI studied; Other drugs provided	Intervention used; Nature of Analysis	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
Scharfstein et al[227]	USA	Mycobacterium avium complex; ZDV and TMP-SMX	Azithromycin, rifabutin and/or clarithromycin commencing at various CD4 counts vs. no MAC prophylaxis; Markov model	Healthcare System; 1995; Fixed and Variable; $ 43,150 - $ 54,450 (depending on strategy)	QALYs	Azithromycin commencing at CD4 count of ≤50	$ 25,000/QALY	All patients were assumed to receive ZDV and TMP-SMX; Several other strategies had lesser effectiveness and higher costs than those shown
						Azithromycin commencing at ≤100 vs. previous strategy	$ 47,000/QALY	
						Azithromycin commencing at ≤200 vs. previous strategy	$ 130,000/QALY	
						Clarithromycin commencing at ≤200 vs. previous strategy	$ 260,000/QALY	Azithromycin and rifabutin vs. this strategy cost $360,000/QALY
4.5.4 CMV Prophylaxis								
Moore & Chaisson[228]	USA	Cytomegalovirus; -	Oral ganciclovir; Markov model	Healthcare System; 1996; Fixed and Variable; $ 104,746	CMV Free Years; QALYs		$ 76,676/QALY $ 37,542/ CMV Free Year	
Paltiel & Freedberg[229]	USA	Cytomegalovirus; ZDV and TMP-SMX	Oral ganciclovir; Markov model	Healthcare System; 1991-2; Fixed and Variable; $54,500	QALYs		$ 159,600/QALY	All patients were assumed to receive ZDV and TMP-SMX
Paltiel et al[230]	USA	Cytomegalovirus; Nothing or ZDV	Oral ganciclovir; Markov model	Healthcare System; 1995; Fixed and Variable; $ 56,700	QALYs		$ 173,000/QALY	
Paltiel et al[231]	USA	Cytomegalovirus; HAART with TMP-SMX and Azithromycin	Oral ganciclovir for all patients or for positive PCR tests; Markov model	Healthcare System; 1998; Fixed and Variable; $ 46,900 - $ 55,600 (depending on strategy)	QALYs	Selective Ganciclovir vs. no prophylaxis	$ 59,000/QALY	Model aimed to pre-emptively predict the results of ACTG A5030
						Comprehensive Ganciclovir vs. no prophylaxis	$ 793,000/QALY	
Rose et al[232]	USA	Cytomegalovirus; ZDV and TMP-SMX	Oral ganciclovir for all patients or for positive PCR tests; Markov model	Programme; 1996; Fixed and Variable; -	Life Years Gained	Selective Ganciclovir vs. no prophylaxis	$ 495,158/LYG	
						Comprehensive Ganciclovir vs. no prophylaxis	$1,762,517/LYG	

Authors	Location	OI studied; Other drugs provided	Intervention used; Nature of Analysis	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
4.5.5 Other OI Prophylaxis								
Scharfstein et al[233]	USA	Primary Systematic Fungal Infections; ZDV and TMP-SMX	Fluconazole commencing at various CD4 counts; Markov model	Healthcare System; 1994; Fixed and Variable; $ 36,900 - $ 41,000 (depending on strategy and nature of disease)	Life Years Gained	Non-endemic fungal infections	$ 240,000/YLG	All patients were assumed to receive ZDV and TMP-SMX
						Endemic infection (twice the incidence)	$ 96,000/LYG	
Goldie et al[234]	USA	Cervical cancer; ZDV, HAART in sensitivity	Screening every 6 or 12 months with Papanicolaou smears or Colposcopy; Markov model	Healthcare System; 1996; Fixed and Variable; $ 72,430 - $ 78,160 (depending on strategy choice and timing)	Life Years Gained; QALYs	Annual pap. smear	$ 12,800/QALY	Annual colposcopy was less effective and more expensive than all pap. smear arms; Semiannual colposcopy cost $375,000 per additional QALY saved compared with semi-annual the annual arm
						Semiannual pap. smear vs. previous strategy	$14,800/QALY	
						Annual pap. smear after 2 initial semi-annual smears vs. previous strategy	$27,600/QALY	
Goldie et al[235]	USA	Anal Squamous Intraepithelial lesions; Nothing or ZDV, HAART in sensitivity	Screening every 6, 12, 24 or 36 months with anal Papanicolaou; Markov model	Healthcare System; 1996; Fixed and Variable; $ 72,630 - $ 76,990 (depending on strategy choice and timing)	Life Years Gained; QALYs	Commencing at CD4 count >500:		When treatment was begun at a CD4 count of between 200 and 500 annual screening was most efficient, costing $23,800 per QALY
						Screening every 24 months;	$ 13,000/QALY	
						Screening every 12 months vs. previous strategy	$ 16,600/QALY	
Marra et al[236]	British Columbia, Canada	Pneumococcal Pneumonia; TMP-SMX	Prescribing vaccine vs. administrating vaccine; Decision model	Programme; 1998; Fixed and Variable; -	Cases of Pneumonia Averted	Administering vaccine at clinic vs. either other arm	Cost-saving	
Rose[237]	USA	Tuberculosis; -	Long and short-course regimes including isoniazid, rifampin and/or pyrazinamide; Markov model	Programme; 1997; Fixed and Variable; -	QALYs	Daily isoniazid, rifabutin & pyrazinamide for 3 months	$ 1,975/QALY	Six of the seven scenarios were cost-saving, with the most efficient being isoniazid daily for 6 months
Bell et al[238]	Uganda	Tuberculosis; None	Long and short-course regimes including isoniazid, rifampin and/or pyrazinamide; Markov model	Societal; 1997; Fixed and Variable; -	QALYs	Isoniazid daily for 6 months	$ 114/QALY	The isoniazid only arm was cost-saving when lost productivity and patient costs were included; All arms were cost-saving when secondary case costs were also included
						Isoniazid & rifabutin daily for 3 months	$ 275/QALY	
						Rifabutin and pyrazinamide twice weekly for 2 months by DOT	$ 260/QALY	

Authors	Location	OI studied; Other drugs provided	Intervention used; Nature of Analysis	Cost: perspective; year; methodology; lifetime treatment cost	Measure of benefit	Interventions compared	Outcome	Comment
Freedberg et al[239]	USA	Pneumocystis Carinii Pneumonia, Toxoplasmosis, Mycobacterium avium complex, Fungal infections, Cytomegalovirus; Nothing or ZDV	TMP-SMX, Azithromycin, Clarithromycin, Rifabutin, Fluconazole, Ganciclovir; Markov model	Healthcare System; 1995; Fixed and Variable; $ 40,786 - $ 46,009 (depending on strategy)	QALYs	TMP-SMX	$ 2,300/QALY	Results were most sensitive to relative rates of infection incidence and regime adherence; Results were not sensitive to using triple therapy as the ART treatment regimen
						TMP-SMX & azithromycin vs. previous strategy	$ 29,000/QALY	
						TMP-SMX & azithromycin & fluconazole vs. previous strategy	$59,000/QALY	
						TMP-SMX & azithromycin & fluconazole & ganciclovir vs. previous strategy	$ 147,000/QALY	
Yazdanpanah et al[240]	France	Pneumocystis Carinii Pneumonia, Toxoplasmosis, Mycobacterium avium complex, Fungal infections, Cytomegalovirus; HAART	TMP-SMX, Azithromycin, Fluconazole, Ganciclovir; Markov model	Healthcare System; 2000; Fixed and Variable; € 187,900 - € 203,600	QALYs	TMP-SMX	€ 18,700/QALY	Only the most efficient strategy for each OI is detailed here
						Add azithromycin vs. previous strategy	€ 23,900/QALY	
						Add fluconazole vs. previous strategy	€ 55,000/QALY	
						Add ganciclovir vs. previous strategy	€ 130,100/QALY	

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organisation (WHO). AIDS Epidemic Update: December 2003. UNAIDS/03.39E. Geneva, Switzerland: UNAIDS/WHO, 2003

2. Beck, EJ. HIV infection and intervention: the first decade. AIDS Care 1991; 3 (3): 295-302

3. Piot P, Zewkie D, Türmen T. HIV/AIDS Prevention and Treatment. Lancet 2002; 360: 86-9

4. World Health Organisation. Treating 3 million by 2005: making it happen: the WHO strategy. Geneva, Switzerland: WHO, 2003

5. Beck EJ, Miner AH. Effectiveness and efficiency in the delivery of HIV services: economic and related considerations. In: Gazzard BG, Johnson M, Miles A, editors. The effective management of HIV/AIDS. UK Key Advances in Clinical Practice. London: Aesculapius Medical Press, 2001: 113-38

6. Drummond MF, O'Brien B, Stoddart GL, et al. Methods for the Economic Evaluation of Health Care Programmes. Oxford: Oxford University Press, 1997

7. Murray CJL, Lopez AD (eds). The Global Burden of Disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Cambridge, Mass.: Harvard School of Public Health, 1996

8. Jack, W. Principles of Health Economics for Developing Countries. Washington, D.C.: World Bank, 1999

9. Pinkerton SD, Holtgrave DR, DiFranceisco W et al. Cost-threshold analyses of the National AIDS Demonstration Research HIV Prevention Interventions. AIDS 2000; 14: 1257-68

10. Laupacis A, Feeny D, Detsky AS et al. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. Can Med Assoc J 1992; 146 (4): 473-81

11. Bramley D, Graves N, Walker D. The cost effectiveness of universal antenatal screening for HIV in New Zealand. AIDS 2003; 17: 741-8

12. World Bank. Country Groups [online]. Available from URL: http://www.worldbank.org/data/countryclass/classgroups.htm [Accessed 2005 Feb 5]

13. World Health Organisation. Macroeconomics and health: Investing in health for economic development. Report of the Commission on Macroeconomics and Health. Geneva: WHO, 2001

14. Moatti JP. Expanding access to Antiretroviral Treatment in the Developing World: the economic rationale. Keynote Lecture: 2nd International IAS Conference on HIV Pathogenesis and Treatment, Paris, France, 13th July 2003.

15. Ades AE, Ratcliffe J, Gibb DM et al. Economic Issues in the Prevention of Vertical Transmission of HIV. Pharmacoeconomics 2000 Jul; 18 (1): 9-22

16. Bardsley-Elliot A, Perry CM. Nevirapine: a Review of its Use in the Prevention and Treatment of Paediatric HIV Infection. Paediatr Drugs 2000 Sept-Oct; 2 (5): 373-407

17. Creese A, Floyd K, Alban A et al. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. Lancet 2002; 359: 1635–42

18. Dabis F, Newell M, Fransen L et al. Prevention of mother-to-child transmission of HIV in developing countries: recommendations for practice. Health Policy Plan 2000; 15 (1): 34-42

19. Freedberg K, Yazdanpanah Y. Cost-effectiveness of HIV Therapies in Resource-Poor Countries. In: Moatti JP, Coriat B, Souteyrand Y et al, editors. Economics of AIDS and Access to HIV/AIDS Care in Developing Countries: Issues and Challenges. Paris: National Agency for AIDS Research, 2003. 267-91

20. Freedberg KA, Paltiel AD. Cost Effectiveness of Prophylaxis for Opportunistic Infections in AIDS. Pharmacoeconomics 1998 Aug; 14 (2): 165-74

21. Hashimoto H, Kapiga SH, Murata Y. Mass treatment with nevirapine to prevent mother-to-child transmission of HIV/AIDS in sub-Saharan African countries. J Obstet Gynaecol Res 2002 Dec; 28 (6): 313-9

22. Holtgrave DR, Qualls NL, Graham JD. Economic Evaluation of HIV Prevention Programs. Annu Rev Public Health 1996; 17: 467-88

23. Kempen JH, Frick KD, Jabs DA. Incremental Cost Effectiveness of Prophylaxis for Cytomegalovirus Disease in Patients with AIDS. Pharmacoeconomics 2001; 19 (12): 1199-1208

24. Kumaranayake L, Watts C. Economic costs of HIV/AIDS prevention activities in sub-Saharan Africa. AIDS 2000; 14 Suppl. 3: S 239-52

25. Kumaranayake L. Cost-effectiveness and Economic Evaluation of HIV/AIDS-Related Interventions: The State of the Art. In: Forsythe S, editor. The State of the Art: AIDS and Economics. Policy Project/International AIDS Economics Network. 64-74. Available from URL: http://www.iaen.org/conferences/stateofepidemic.php [Accessed 2003 Dec 5]

26. Langtry HD, Palmer KJ, Benfield P. Zidovudine: a review of pharmacoeconomic and quality-of-life considerations for its use in patients with human immunodeficiency virus. Pharmacoeconomics 1993 Apr; 3 (4): 309-37

27. Lynn LA, Schulman KA, Eisenberg JM. The pharmacoeconomics of HIV disease. Pharmacoeconomics 1992 Mar; 1(3): 161-74

28. Malek M, Davey P. Economics of mandatory HIV and hepatitis B virus testing for healthcare workers performing surgical procedures. Pharmacoeconomics 1993 Dec; 4 (6): 401-4

29. Moore RD. Cost Effectiveness of Combination HIV Therapy: 3 Years Later. Pharmacoeconomics 2000 Apr; 17 (4): 325-30

30. Newell M, Dabis F, Tolley K et al. Cost-effectiveness and cost-benefit in the prevention of mother-to-child transmission of HIV in developing countries. AIDS 1998; 12: 1571-80

31. Pinkerton SD, Holtgrave DR, Willingham M et al. Cost-Effectiveness and HIV Prevention Community Planning. AIDS Public Policy J 1998 Fall; 13 (3): 115-27

32. Pinkerton SD, Johnson-Masotti AP, Holtgrave DR et al. Using cost-effectiveness league tables to compare interventions to prevent sexual transmission of HIV. AIDS 2001; 15: 917-28

33. Read JS. Cesarean Section Delivery to Prevent Vertical Transmission of Human Immunodeficiency Virus Type 1: Associated Risks and Other Considerations. Ann N Y Acad Sci 2000 Nov; 918: 115-21

34. Schrappe M, Lauterbach K. Systematic review on the cost-effectiveness of public health interventions for HIV prevention in industrialized countries. AIDS 1998; 12 Suppl. A: S231-8

35. Scotland GS, van Teijlingen ER, van der Pol M et al. A review of studies assessing the costs and consequences of interventions to reduce mother-to-child HIV transmission in sub-Saharan Africa. AIDS 2003; 17: 1045-1052

36. Walker D. Cost and cost-effectiveness of HIV/AIDS prevention strategies in developing countries: is there an evidence base? Health Policy Plan 2003; 18 (1): 4-17

37. Youle M, Trueman P, Simpson K. Health Economics in HIV Disease. Pharmacoeconomics 1999; 15 Suppl. 1: 1-12

38. Allen UD, Read S, Gafni A. Zidovudine for chemoprophylaxis after occupational exposure to HIV-infected blood: an economic evaluation. Clin Infect Dis Apr 1992; 14 (4): 822-30

39. Cantor SB. Carson RW. Spann SJ. A cost-effectiveness analysis of epoetin usage for patients with AIDS. Pharmacoeconomics 1993 Mar; 3 (3): 244-9

40. Crystal S, Dengelegi L, Beck P et al. AIDS contact notification: initial program results in New Jersey. AIDS Educ Prev 1990; 2 (4): 284-95

41. Cummins L. Compulsory premarital screening for HIV. JAMA 1988 Feb 19; 259: 1012-3

42. Giesecke J, Ramstedt K, Granath F, et al. Efficacy of partner notification for HIV infection. Lancet 1991 Nov 2; 338: 1096-100

43. Johanson JF, Sonnenberg A. Efficient management of diarrhea in the acquired immunodeficiency syndrome (AIDS): A medical decision analysis. Ann Intern Med 1990 Jun 15; 112 (12): 942-8

44. McKay NL, Phillips KM. An economic evaluation of mandatory premarital testing for HIV. Inquiry 1991 Fall; 28 (3): 236-48

45. Mendelson DN, Sandler SG. A model for estimating incremental benefits and costs of testing donated blood for human immunodeficiency virus antigen (HIV-Ag). Transfusion 1990 Jan; 30 (1): 73-5

46. Oddone EZ, Cowper P, Hamilton JD et al. Cost effectiveness analysis of early zidovudine treatment of HIV infected patients. Br Med J 1993 Nov 20; 307: 1322-5

47. Paltiel AD, Kaplan EH. Modeling zidovudine therapy: a cost-effectiveness analysis. J Acquir Immune Defic Syndr 1991; 4 (8): 795-804

48. Petersen LR, White CR. Premarital Screening for Antibodies to Human Immunodeficiency Virus Type 1 in the United States. Am J Public Health 1990; 80: 1087-90

49. Ramsey SD, Nettleman MD. Cost-effectiveness of prophylactic AZT following needlestick injury in health care workers. Med Decis Making 1992 Apr-Jun; 12 (2): 142-8

50. Rose DN, Schechter CB, Sacks HS. Influenza and pneumococcal vaccination of HIV-infected patients: a policy analysis. Am J Med 1993 Feb; 94 (2): 160-8

51. Russo G, La Croix SJ. A second look at the cost of mandatory human immunodeficiency virus and hepatitis B virus testing for healthcare workers performing invasive procedures. Infect Control Hosp Epidemiol 1992 Feb; 13 (2): 107-10

52. Rutherford GW, Woo JM, Neal DP. Partner Notification and the control of human immunodeficiency virus infection: two years of experience in San Francisco. Sex Transm Dis 1991; 18: 107-10

53. Schulman KA, Lynn LA, Glick HA et al. Cost effectiveness of low-dose zidovudine therapy for asymptomatic patients with human immunodeficiency virus (HIV) infection. Ann Intern Med 1991 May 1; 114 (9): 798-802

54. Spencer NE, Hoffman RE, Raevsky CA. Partner notification for human immunodeficiency virus infection in Colorado: results across index case groups and costs. Int J STD AIDS 1993; 4: 26-32

55. Stock SR, Gafni A, Bloch RF. Universal precautions to prevent HIV transmission to health care workers: an economic analysis. Can Med Assoc J 1990 May 1; 142 (9): 937-46

56. Turnock BJ, Kelly CJ. Mandatory Premarital Testing for Human Immunodeficiency Virus: the Illinois Experience. JAMA 1989; 261: 3415-8

57. Wykoff RF, Heath CW Jr, Hollis SL et al. Contact tracing to identify human immunodeficiency virus infection in a rural community. JAMA 1988 Jun 24; 259 (24): 3563-6

58. Yawn, BP. Clinical Decision Analysis of HIV Screening. Fam Med 1992; 24: 355-61

59. Villari P, Fattore G, Siegel JE et al. Economic evaluation of HIV testing among intravenous drug users: An analytic framework and its application to Italy. International Journal of Technology Assessment in Health Care 1996 Spring; 12 (2): 336-57

60. Holtgrave DR, Pinkerton SD, Jones TS et al. Cost and cost-effectiveness of increasing access to sterile syringes and needles as an HIV prevention intervention in the United States. J Acquir Immune Defic Syndr Hum Retrovirol 1998; 18 Suppl. 1: S133-8

61. Laufer FN. Cost-effectiveness of syringe exchange as an HIV prevention strategy. J Acquir Immune Defic Syndr 2001 Nov 1; 28 (3): 273-8

62. Gold M, Gafni A, Nelligan P, et al. Needle exchange programs: an economic evaluation of a local experience. Can Med Assoc J 1997; 157: 255-262

63. Jacobs P, Calder P, Taylor M et al. Cost effectiveness of Streetworks' needle exchange program of Edmonton. Can J Public Health 1999 May-Jun; 90 (3): 168-71

64. Zaric GS, Barnett PG, Brandeau ML. HIV transmission and the cost-effectiveness of methadone maintenance. J Acquir Immune Defic Syndr 2000 Dec 15; 25 (5): 403-16

65. Laufer FN, Chiarello LA. Application of cost-effectiveness methodology to the consideration of needlestick-prevention technology. Am J Infect Control 1994 Apr; 22 (2): 75-82

66. Dziekan G, Chisholm D, Johns B et al. The cost-effectiveness of policies for the safe and appropriate use of injection in healthcare settings. Bull World Health Organ 2003; 81 (4): 277-85

67. Chesson HW, Greenberg JB, Hennessy M. The cost-effectiveness of the WINGS intervention: a program to prevent HIV and sexually transmitted diseases among high-risk urban women. BMC Infect Dis 2002 Oct 11; 2 (1): 24

68. Holtgrave DR, Kelly JA. Preventing HIV/AIDS among high-risk urban women: the cost-effectiveness of a behavioral group intervention. Am J Public Health 1996 Oct; 86 (10): 1442-5

69. Moses S, Plummer FA, Ngugi EN et al. Controlling HIV in Africa: effectiveness and cost of an intervention in a high-frequency STD transmitter core group. AIDS 1991 Apr; 5 (4): 407-11

70. Marseille E, Kahn JG, Billinghurst K et al. Cost-effectiveness of the female condom in preventing HIV and STDs in commercial sex workers in rural South Africa. Soc Sci Med 2001 Jan; 52 (1): 135-48

71. Pinkerton SD, Holtgrave DR, DiFranceisco WJ et al. Cost-effectiveness of a community-level HIV risk reduction intervention. Am J Public Health 1998 Aug; 88 (8): 1239-42

72. Kahn JG, Kegeles SM, Hays R et al. Cost-effectiveness of the Mpowerment Project, a community-level intervention for young gay men. J Acquir Immune Defic Syndr 2001 Aug 15; 27 (5): 482-91

73. Tao G, Remafedi G. Economic evaluation of an HIV prevention intervention for gay and bisexual male adolescents. J Acquir Immune Defic Syndr Hum Retrovirol 1998 Jan 1; 17 (1): 83-90

74. Holtgrave DR, Kelly JA. Cost-effectiveness of a cognitive-behavioral, HIV prevention intervention for gay men. AIDS & Behav 1997; 1: 173-80

75. Pinkerton SD, Holtgrave DR, Valdiserri RO. Cost-effectiveness of HIV-prevention skills training for men who have sex with men. AIDS 1997 Mar; 11 (3): 347-57

76. Johnson-Masotti AP, Pinkerton SD, Kelly JA et al. Cost-effectiveness of an HIV risk reduction intervention for adults with severe mental illness. AIDS Care 2000 Jun; 12 (3): 321-32

77. Pinkerton SD, Johnson-Masotti AP, Otto-Salaj LL et al. Cost-effectiveness of an HIV prevention intervention for mentally ill adults. Ment Health Serv Res 2001 Mar; 3 (1): 45-55

78. Sweat M, O'Donnell C, O'Donnell L. Cost-effectiveness of a brief video-based HIV intervention for African American and Latino sexually transmitted disease clinic clients. AIDS 2001 Apr 13; 15 (6): 781-7

79. Wang LY, Davis M, Robin L et al. Economic evaluation of Safer Choices: a school-based human immunodeficiency virus, other sexually transmitted diseases, and pregnancy prevention program. Arch Pediatr Adolesc Med 2000 Oct; 154 (10): 1017-24

80. Heumann KS, Marx R, Lawrence SJ et al. Cost-effectiveness of prevention referrals for high-risk HIV-negatives in San Francisco. AIDS Care 2001 Oct; 13 (5): 637-42

81. Pinkerton SD, Holtgrave DR, Jemmott JB 3rd. Economic evaluation of HIV risk reduction intervention in African-American male adolescents. J Acquir Immune Defic Syndr 2000 Oct 1; 25 (2): 164-72

82. Pinkerton SD, Holtgrave DR, Johnson-Masotti AP et al. Cost-effectiveness of the NIMH multisite HIV prevention intervention. AIDS Behav 2002 Mar; 6 (1): 83-96

83. Bedimo AL, Pinkerton SD, Cohen DA et al. Condom distribution: a cost-utility analysis. Int J STD AIDS 2002 Jun; 13 (6): 384-92

84. Pinkerton SD, Abramson PR, Holtgrave DR. What is a Condom worth? AIDS Behav 1999; 3 (4): 301-12

85. Hughes D, Morris S. The cost-effectiveness of condoms in the prevention of HIV infection in England and Wales: should condoms be available on prescription? J Health Serv Res Policy 1996 Oct; 1 (4): 205-11

86. Holtgrave DR. Estimating the effectiveness and efficiency of US HIV prevention efforts using scenario and cost-effectiveness analysis. AIDS 2002 Nov 22; 16 (17): 2347-9

87. Holtgrave DR, Pinkerton SD. Economic implications of failure to reduce incident HIV infections by 50% by 2005 in the United States. J Acquir Immune Defic Syndr 2003; 33: 171-4

88. Gilson L, Mkanje R, Grosskurth H et al. Cost-effectiveness of improved treatment services for sexually transmitted diseases in preventing HIV-1 infection in Mwanza Region, Tanzania. Lancet 1997 Dec 20-27; 350: 1805-9

89. Rahman M, Fukui T, Asai A. Cost-effectiveness analysis of partner notification program for human immunodeficiency virus infection in Japan. J Epidemiol 1998 Jun; 8 (2): 123-8

90. Cowley P. Preliminary cost-effectiveness analysis of an AIDS vaccine in Abidjan, Ivory Coast. Health Policy 1993 May; 24 (2): 145-53

91. Bos JM, Postma MJ. The economics of HIV vaccines: projecting the impact of HIV vaccination of infants in sub-Saharan Africa. Pharmacoeconomics 2001; 19 (9): 937-46

92. Kahn JG, Sanstad KC. The role of cost-effectiveness analysis in assessing HIV-prevention interventions. AIDS Public Policy J 1997 Spring; 12 (1): 21-30

93. Over M, Piot P. Human immunodeficiency virus infection and other sexually transmitted diseases in developing countries: public health importance and priorities for resource allocation. J Infect Dis 1996 Oct; 174 Suppl. 2: S162-75

94. Hutton G, Wyss K, N'Diékhor Y. Prioritization of prevention activities to combat the spread of HIV/AIDS in resource constrained settings: a cost-effectiveness analysis from Chad, Central Africa. Int J Health Plann Manage 2003; 18: 117-36

95. Brandeau ML, Owens DK, Sox CH et al. Screening women of childbearing age for human immunodeficiency virus: A cost-benefit analysis. Arch Intern Med 1992 Nov; 152 (11): 2229-37

96. Houshyar A. Screening pregnant women for HIV antibody: cost-benefit analysis. AIDS Public Policy J 1991 Summer; 6 (2): 98-103

97. Le Gales C, Moatti JP. Cost-effectiveness of HIV screening of pregnant women in hospitals of the Paris area: the Paris-Tours study group of antenatal transmission of HIV, Group '9 maternities'. Eur J Obstet Gynecol Reprod Biol 1990 Oct; 37 (1): 25-33

98. Henry K, Campbell S. The Potential Efficiency of Routine HIV Testing of Hospital Patients - Data from a CDC Sentinel Hospital. Public Health Rep 1992; 107: 138-41

99. Lurie P, Avins AL, Phillips KA et al. The cost-effectiveness of voluntary counseling and testing of hospital inpatients for HIV infection. JAMA 1994 Dec 21; 272 (23): 1832-8

100. Owens DK, Nease RF Jr, Harris RA. Cost-effectiveness of HIV screening in acute care settings. Arch Intern Med 1996 Feb 26; 156 (4): 394-404

101. La Croix SJ, Russo G. A cost-benefit analysis of voluntary routine HIV-antibody testing for hospital patients. Soc Sci Med 1996 May; 42 (9): 1259-72

102. Wilkinson D, Wilkinson N, Lombard C. On-site HIV testing in resource-poor settings: is one rapid test enough? AIDS 1997; 11(3): 377-81

103. Mullins JR, Harrison PB. The Questionable Utility of Mandatory Screening for the Human Immunodeficiency Virus. Am J Surgery 1993; 166: 676-79

104. Mathoulin-Pelissier S, Salmi LR, Fialon P et al. Cost-effectiveness of testing for human immunodeficiency virus and hepatitis C virus among blood transfusion recipients. Infect Control Hosp Epidemiol 2003 Feb; 24 (2): 132-6

105. Wallace SV, Carlin EM. HIV in cervical cancer. Int J STD AIDS 2001 May; 12 (5): 283-5

106. Mrus JM, Yi MS, Eckman MH et al. The impact of expected HIV transmission rates on the effectiveness and cost of ruling out HIV infection in infants. Med Decis Making 2002 Sep-Oct; 22 (5 Suppl.): S38-44

107. Chavey WE, Cantor SB, Clover RD et al. Cost-effectiveness analysis of screening health care workers for HIV. J Fam Pract 1994 Mar; 38 (3): 249-57

108. Owens DK, Harris RA, Scott PM et al. Screening surgeons for HIV infection: a cost-effectiveness analysis. Ann Intern Med 1995 May 1; 122 (9): 641-52

109. Sell RL, Jovell AJ, Siegel JE. HIV screening of surgeons and dentists: a cost-effectiveness analysis. Infect Control Hosp Epidemiol 1994 Oct; 15 (10): 635-45

110. Phillips KA, Lowe RA, Kahn JG et al. The cost-effectiveness of HIV testing of physicians and dentists in the United States. JAMA 1994 Mar 16; 271 (11): 851-8

111. Varghese B, Peterman TA, Holtgrave DR. Cost-effectiveness of counseling and testing and partner notification: a decision analysis. AIDS 1999 Sep 10; 13 (13): 1745-51

112. Bos JM, Fennema JS, Postma MJ. Cost-effectiveness of HIV screening of patients attending clinics for sexually transmitted diseases in Amsterdam. AIDS 2001 Oct 19; 15 (15): 2031-6

113. Bos JM, van der Meijden WI, Swart W et al. Routine HIV screening of sexually transmitted disease clinic attenders has favourable cost-effectiveness ratio in low HIV prevalence settings. AIDS 2002 May 24; 16 (8): 1185-7

114. Farnham PG, Gorsky RD, Holtgrave DR et al. Counseling and testing for HIV prevention: costs, effects, and cost-effectiveness of more rapid screening tests. Public Health Rep 1996 Jan-Feb; 111 (1): 44-53

115. Holtgrave DR, Valdiserri RO, Gerber AR et al. Human immunodeficiency virus counseling, testing, referral, and partner notification services: A cost-benefit analysis. Arch Intern Med 1993 May 24; 153 (10): 1225-30

116. Phillips KA, Fernyak S. The cost-effectiveness of expanded HIV counselling and testing in primary care settings: a first look. AIDS 2000 Sep 29; 14 (14): 2159-69

117. Sweat M, Gregorich S, Sangiwa G et al. Cost-effectiveness of voluntary HIV-1 counselling and testing in reducing sexual transmission of HIV-1 in Kenya and Tanzania. Lancet 2000 Jul 8; 356: 113-21

118. Bloom DE, Glied S. Benefits and costs of HIV testing. Science 1991 Jun 28; 252: 1798-804

119. Zowall H, Fraser RD, Gilmore N et al. HIV antibody screening among immigrants: a cost-benefit analysis. Can Med Assoc J 1990 Jul 15; 143 (2): 101-7

120. Gorsky RD, MacGowan RJ, Swanson NM, et al. Prevention of HIV infection in drug abusers: a cost analysis. Prev Med 1995 Jan; 24 (1): 3-8

121. Varghese B, Peterman TA. Cost-effectiveness of HIV counseling and testing in US prisons. J Urban Health 2001 Jun; 78 (2): 304-12

122. Blaxhult A, Anagrius C, Arneborn M et al. Evaluation of HIV testing in Sweden, 1985-1991. AIDS 1993 Dec; 7 (12): 1625-31

123. Eisenstaedt RS, Getzen TE. Screening blood donors for human immunodeficiency virus antibody: cost-benefit analysis. Am J Public Health 1988 Apr; 78 (4): 450-4

124. Schwartz JS, Kinosian BP, Pierskalla WP, et al. Strategies for Screening Blood for Human Immunodeficiency Virus Antibody: Use of a Decision Support System. JAMA 1990; 264 (13): 1704-10

125. Gelles GM. Costs and benefits of HIV-1 antibody testing of donated blood. J Policy Anal Manage 1993 Summer; 12 (3): 512-31

126. AuBuchon JP, Birkmeyer JD, Busch MP. Cost-effectiveness of expanded human immunodeficiency virus-testing protocols for donated blood. Transfusion 1997 Jan; 37 (1): 45-51

127. Jackson BR, Busch MP, Stramer SL, et al. The cost-effectiveness of NAT for HIV, HCV and HBV in whole-blood donations. Transfusion 2003; 43: 721-9

128. Busch MP, Dodd RY, Lackritz EM et al. on behalf of the HIV Blood Donor Study Group. Value and cost-effectiveness of screening blood donors for antibody to hepatitis B core antigen as a way of detecting window-phase human immunodeficiency virus type 1 infections. Transfusion 1997 Oct; 37 (10): 1003-11

129. Sailly JC, Lebrun T, Coudeville L. Evaluation of the cost-effectiveness ratio of HIV, HVB, HCV, HTLV screening associated with blood transfusion in France [in French]. Rev Epidemiol Sante Publique 1997 Apr; 45 (2): 131-41

130. Djossou F, Salmi LR, Lawson-Ayayi S et al. A cost-effectiveness analysis of screening strategies for human immunodeficiency virus in donated blood in France [in French]. Transfus Clin Biol 1999 Jun; 6 (3): 180-8

131. Watson-Williams EJ, Kataah PK. Revival of the Ugandan Blood Transfusion System 1989: an example of International Cooperation. Transfus Sci 1990; 11: 179-84

132. Laleman G, Magazani K, Perriens JH et al. Prevention of blood-borne HIV transmission using a decentralized approach in Shaba, Zaire. AIDS 1992 Nov; 6 (11): 1353-8

133. Foster S, Buvé A. Benefits of HIV screening of blood transfusions in Zambia. Lancet 1995 Jul 22; 346: 225-7

134. Jacobs B, Mercer A. Feasibility of hospital-based blood banking: a Tanzanian case study. Health Policy Plan 1999 Dec; 14 (4): 354-62

135. McFarland W, Kahn JG, Katzenstein DA et al. Deferral of blood donors with risk factors for HIV infection saves lives and money in Zimbabwe. J Acquir Immune Defic Syndr Hum Retrovirol 1995 Jun 1; 9 (2): 183-92

136. AuBuchon JP, Birkmeyer JD. Safety and cost-effectiveness of solvent-detergent-treated plasma. In search of a zero-risk blood supply. JAMA 1994 Oct 19; 272 (15): 1210-4

137. Pereira A. Cost-effectiveness of transfusing virus-inactivated plasma instead of standard plasma. Transfusion 1999 May; 39 (5): 479-87

138. Etchason J, Petz L, Keeler E et al. The Cost Effectiveness of Preoperative Autologous Blood Donations. N Engl J Med 1995; 332: 719-24

139. Gorsky RD, Farnham PG, Straus WL et al. Preventing perinatal transmission of HIV--costs and effectiveness of a recommended intervention. Public Health Rep 1996 Jul-Aug 111 (4): 335-41

140. Grobman WA, Garcia PM. The cost-effectiveness of voluntary intrapartum rapid human immunodeficiency virus testing for women without adequate prenatal care. Am J Obstet Gynecol 1999 Nov; 181 (5 Pt 1): 1062-71

141. Lewis R, O'Brien JM, Ray DT, et al. The impact of initiating a human immunodeficiency virus screening program in an urban obstetric population. Am J Obstet Gynecol 1995; 173 (4): 1329-1333

142. Mauskopf JA, Paul JE, Wichman DS et al. Economic Impact of Treatment of HIV-Positive Pregnant Women and Their Newborns with Zidovudine. JAMA 1996 Jul 10; 276 (2): 132-8

143. Patrick DM, Money DM, Forbes J et al. Routine prenatal screening for HIV in a low-prevalence setting. Can Med Assoc J 1998 Oct 20; 159 (8): 942-7

144. Postma MJ, Beck EJ, Mandalia S et al. Universal HIV screening of pregnant women in England: cost effectiveness analysis. Br Med J 1999 Jun 19; 318: 1656-60

145. Ecker JL. The cost-effectiveness of human immunodeficiency virus screening in pregnancy. Am J Obstet Gynecol 1996 Feb; 174 (2): 716-21

146. Dunn DT, Nicoll A, Holland FJ, et al. How much paediatric HIV infection could be prevented by antenatal HIV testing? J Med Screen 1995; 2 (1): 35-40

147. Mansergh G, Haddix AC, Steketee RW et al. Cost-effectiveness of short-course zidovudine to prevent perinatal HIV type 1 infection in a sub-Saharan African Developing country setting. JAMA 1996 Jul 10; 276 (2): 139-45

148. Mansergh G, Haddix AC, Steketee RW et al. Cost-effectiveness of zidovudine to prevent mother-to-child transmission of HIV in sub-Saharan Africa. JAMA 1998 Jul 1; 280 (1): 30-1

149. Marseille E, Kahn JG, Mmiro F et al. Cost effectiveness of single-dose nevirapine regimen for mothers and babies to decrease vertical HIV-1 transmission in sub-Saharan Africa. Lancet 1999 Sep 4; 354: 803-9

150. Wilkinson D, Floyd K, Gilks CF. Antiretroviral drugs as a public health intervention for pregnant HIV-infected women in rural South Africa: an issue of cost-effectiveness and capacity. AIDS 1998 Sep 10; 12 (13): 1675-82

151. Wilkinson D, Floyd K, Gilks CF. National and provincial estimated costs and cost effectiveness of a programme to reduce mother-to-child HIV transmission in South Africa. S Afr Med J 2000 Aug; 90 (8): 794-8

152. Skordis J, Nattrass N. Paying to waste lives: the affordability of reducing mother-to-child transmission of HIV in South Africa. J Health Econ 2002 May; 21 (3): 405-21

153. Wood E, Braitstein P, Montaner JS et al. Extent to which low-level use of antiretroviral treatment could curb the AIDS epidemic in sub-Saharan Africa. Lancet 2000 Jun 17; 355: 2095-100

154. Söderlund N, Zwi K, Kinghorn A et al. Prevention of vertical transmission of HIV: analysis of cost effectiveness of options available in South Africa. Br Med J 1999 Jun 19; 318: 1650-6

155. Marseille E, Kahn JG, Saba J. Cost-effectiveness of antiviral drug therapy to reduce mother-to-child HIV transmission in sub-Saharan Africa. AIDS 1998 May; 12 (8): 939-48

156. Pinkerton SD, Holtgrave DR, Layde PM. Incremental cost-effectiveness of two zidovudine regimens to prevent perinatal HIV transmission in the United States. Prev Med 2000 Jan 30 (1): 64-9

157. Myers ER, Thompson JW, Simpson K. Cost-effectiveness of mandatory compared with voluntary screening for human immunodeficiency virus in pregnancy. Obstet Gynecol 1998 Feb; 91 (2): 174-81

158. Immergluck LC, Cull WL, Schwartz A et al. Cost-effectiveness of universal compared with voluntary screening for human immunodeficiency virus among pregnant women in Chicago. Pediatrics 2000 Apr; 105 (4): E54

159. Zaric GS, Bayoumi AM, Brandeau ML et al. The cost effectiveness of voluntary prenatal and routine newborn HIV screening in the United States. Am J Public Health 2000; 90: 1100-11

160. Chen KT, Sell RL, Tuomala RE. Cost-effectiveness of elective cesarean delivery in human immunodeficiency virus-infected women. Obstet Gynecol 2001 Feb; 97 (2): 161-8

161. Mrus JM, Goldie SJ, Weinstein MC et al. The cost-effectiveness of elective Cesarean delivery for HIV-infected women with detectable HIV RNA during pregnancy. AIDS 2000 Nov 10; 14 (16): 2543-52

162. Halpern MT, Read JS, Ganoczy DA et al. Cost-effectiveness of cesarean section delivery to prevent mother-to-child transmission of HIV-1. AIDS 2000 Apr 14; 14 (6): 691-700

163. Stringer JS, Rouse DJ. Rapid testing and zidovudine treatment to prevent vertical transmission of human immunodeficiency virus in unregistered parturients: a cost-effectiveness analysis. Obstet Gynecol 1999 Jul; 94 (1): 34-40

164. Stringer JS, Rouse DJ, Vermund SH et al. Cost-effective use of nevirapine to prevent vertical HIV transmission in sub-Saharan Africa. J Acquir Immune Defic Syndr 2000 Aug 1; 24 (4): 369-77

165. Rely K, Bertozzi SM, Avila-Figueroa C et al. Cost-effectiveness of strategies to reduce mother-to-child HIV transmission in Mexico, a low-prevalence setting. Health Policy Plan 2003 Sep; 18 (3): 290-8

166. Ratcliffe J, Ades AE, Gibb D et al. Prevention of mother-to-child transmission of HIV-1 infection: alternative strategies and their cost-effectiveness. AIDS 1998 Jul 30; 12 (11): 1381-8

167. Postma MJ, Beck EJ, Hankins CA, et al. Cost effectiveness of expanded antenatal HIV testing in London. AIDS 2000 Oct 20; 14 (15): 2383-9

168. Sansom SL, Jamieson DJ, Farnham PG et al. Human Immunodeficiency Virus retesting during pregnancy: costs and effectiveness in preventing perinatal transmission. Obstet Gynecol 2003; 102: 782-90

169. Connor EM, Sperling RS, Gelber R et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N Engl J Med 1994; 331: 1173-80

170. Shaffer N, Chuachoowong R, Mock PA et al. Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. Lancet 1999; 353: 773-80

171. Wiktor S, Ekpini E, Karon JM. Short-course oral zidovudine for prevention of mother-to-child transmission of HIV-1 in Abidjan, Côte D'Ivoire: a randomised trial. Lancet 1999; 353: 781-5

172. European Collaborative Study. Caesarean section and risk of vertical transmission of HIV-1 infection. Lancet 1994; 343: 1464-7

173. Guay LA, Musoke PM, Flemming T et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. Lancet 1999 Sep 4; 354: 705-802

174. Saba J. UNAIDS, 6th Conference on retroviruses and opportunistic infections, Jan 31-Feb 4. Chicago, 1999.

175. Wade NA, Birkhead GS, Warren BL et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. N Engl J Med 1998 Nov 12; 339(20): 1409-14

176. Cooper ER, Charurat M, Mofenson L et al. Combination Antiretroviral Strategies for the Treatment of Pregnant HIV-1-Infected Women and Prevention of Perinatal HIV-1 Transmission. J Acquir Immune Defic Syndr 2002; 29: 484-94

177. Moore RD, Hidalgo J, Bareta JC et al. Zidovudine therapy and health resource utilization in AIDS. J Acquir Immune Defic Syndr 1994 Apr; 7 (4): 349-54

178. Messori A, Becagli P, Berto V et al. on behalf of the Osservatorio SIFO sui Farmaci. Advanced HIV infection treated with zidovudine monotherapy: lifetime values of absolute cost-effectiveness as a pharmacoeconomic reference for future studies evaluating antiretroviral combination treatments. Ann Pharmacother 1997 Dec; 31 (12): 1447-54

179. McCarthy BD, Wong JB, Munoz A et al. Who should be screened for HIV infection? A cost-effectiveness analysis. Arch Intern Med 1993 May 10; 153 (9): 1107-16

180. Lacey L, Mauskopf J, Lindrooth R et al. A prospective cost-consequence analysis of adding lamivudine to zidovudine-containing antiretroviral treatment regimens for HIV infection in the US. Pharmacoeconomics 1999; 15 Suppl. 1: 23-37

181. Lacey L, Youle M, Trueman P et al. A prospective evaluation of the cost effectiveness of adding lamivudine to zidovudine-containing antiretroviral treatment regimens in HIV infection: European perspective. Pharmacoeconomics 1999; 15 Suppl. 1: 39-53

182. Lacey L, Hopkinson PK, Montaner J et al. An evaluation of the cost effectiveness of adding lamivudine to zidovudine-containing regimens in HIV infection: Canadian perspective. Pharmacoeconomics 1999; 15 Suppl. 1: 55-66

183. Simpson K, Hatziandreu EJ, Andersson F et al. Cost effectiveness of antiviral treatment with zalcitabine plus zidovudine for AIDS patients with CD4+ counts less than 300/microliters in 5 European countries. Pharmacoeconomics 1994 Dec; 6 (6): 553-62

184. Chancellor JV, Hill AM, Sabin CA et al. Modelling the cost effectiveness of lamivudine/zidovudine combination therapy in HIV infection. Pharmacoeconomics 1997 Jul; 12 (1): 54-66

185. Davies D, Carne C, Camilleri-Ferrante C. Combined antiretroviral treatment in HIV infection: Is it value for money? Public Health 1999; 113: 315-7

186. Mauskopf J, Lacey L, Kempel A et al. The cost-effectiveness of treatment with lamivudine and zidovudine compared with zidovudine alone: a comparison of Markov model and trial data estimates. Am J Manage Care 1998 Jul; 4 (7): 1004-12

187. Freedberg KA, Losina E, Weinstein MC et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. N Engl J Med 2001 Mar 15; 344 (11): 824-31

188. Sendi PP, Bucher HC, Harr T et al. on behalf of the Swiss HIV Cohort Study. Cost effectiveness of highly active antiretroviral therapy in HIV-infected patients. AIDS 1999 Jun 19; 13 (9): 1115-22

189. Schackman BR, Goldie SJ, Weinstein MC et al. Cost-effectiveness of earlier initiation of antiretroviral therapy for uninsured HIV-infected adults. Am J Public Health 2001 Sep; 91 (9): 1456-63

190. Schackman BR, Freedberg KA, Weinstein MC et al. Cost-effectiveness implications of the timing of antiretroviral therapy in HIV-infected adults. Arch Intern Med 2002 Nov 25; 162 (21): 2478-86

191. Schackman BR, Goldie SJ, Freedberg KA et al. Comparison of health state utilities using community and patient preference weights derived from a survey of patients with HIV/AIDS. Med Decis Making 2002 Jan-Feb 22 (1): 27-38

192. Moore RD, Bartlett JG. Combination antiretroviral therapy in HIV infection. An economic perspective. Pharmacoeconomics 1996 Aug; 10 (2): 109-13

193. Cook J, Dasbach E, Coplan P et al. Modeling the long-term outcomes and costs of HIV antiretroviral therapy using HIV RNA levels: application to a clinical trial. AIDS Res Hum Retroviruses 1999 Apr 10; 15 (6): 499-508

194. Miners AH, Sabin CA, Trueman P et al. Assessing the cost-effectiveness of HAART for adults with HIV in England. HIV Med 2001 Jan; 2 (1): 52-8

195. Trueman P, Youle M, Sabin CA et al. The cost-effectiveness of triple nucleoside analogue therapy antiretroviral regimens in the treatment of HIV in the United Kingdom. HIV Clin Trials 2000 Jul-Aug; 1 (1): 27-35

196. Anis AH, Guh D, Hogg RS et al. The cost-effectiveness of antiretroviral regimens for the treatment of HIV/AIDS. Pharmacoeconomics 2002 Oct; 18 (4): 393-404

197. Pinkerton SD, Holtgrave DR, Pinkerton HJ. Cost-effectiveness of chemoprophylaxis after occupational exposure to HIV. Arch Intern Med 1997 Sep 22; 157 (17): 1972-80

198. Marin MG, Van Lieu J, Yee A et al. Cost-effectiveness of a post-exposure HIV chemoprophylaxis program for blood exposures in health care workers. J Occup Environ Med 1999 Sep; 41 (9): 754-60

199. Li RW, Wong JB. Postexposure treatment of HIV. NEJM 1997 Aug 14; 337 (7): 499-500

200. King AM, Osterwalder JJ, Vernazza PL. A randomised prospective study to evaluate a rapid HIV-antibody assay in the management of cases of percutaneous exposure amongst health care workers. Swiss Med Wkly 2001 Jan 12; 131 (1-2): 10-3

201. Lurie P, Miller M, Hecht F et al. Postexposure Prophylaxis After Nonoccupational HIV Exposure: Clinical, Ethical, and Policy Considerations. JAMA 1998; 280: 1769-73

202. Pinkerton SD, Holtgrave DR, Bloom FR. Cost-effectiveness of post-exposure prophylaxis following sexual exposure to HIV. AIDS 1998 Jun 18; 12 (9): 1067-78

203. Pinkerton, Holtgrave DR, Bloom FR. Postexposure treatment of HIV. NEJM 1997 Aug 14; 337 (7): 500-1

204. Wallace MR, Tasker SA, Shinohara YT et al. The changing economics of HIV care. AIDS Patient Care STDS 2001 Jan; 15 (1): 25-9

205. Boulle A, Kenyon C, Skordis J et al. Exploring the costs of a limited public sector antiretroviral treatment programme in South Africa. S Afr Med J 2002 Oct; 92 (10): 811-7

206. Caro JJ, O'Brien JA, Migliaccio-Walle K. Economic analysis of initial HIV treatment: efavirenz- versus indinavir-containing triple therapy. Pharmacoeconomics 2001; 19(1): 95-104

207. Tramarin A, Milocchi F, Tolley K et al. An economic evaluation of home-care assistance for AIDS patients: a pilot study in a town in northern Italy. AIDS 1992 Nov; 6 (11): 1377-83

208. McCue MJ, Mazmanian PE, Hampton C et al. The case of Powhatan Correctional Center/Virginia Department of Corrections and Virginia Commonwealth University/Medical College of Virginia. Telemed Journal 1997 Spring; 3 (1): 11-7

209. Gibb DM, Ades AE, Gupta R et al. Costs and benefits to the mother of antenatal HIV testing: estimates from simulation modelling. AIDS 1999 Aug 20; 13 (12): 1569-76

210. Allen UD, Kirby MA, Goeree R. Cost-effectiveness of recombinant human erythropoietin versus transfusions in the treatment of zidovudine-related anemia in HIV-infected children. Pediatr AIDS HIV Infect 1997 Feb; 8 (1): 4-11

211. Weinstein MC, Goldie SJ, Losina E et al. Use of genotypic resistance testing to guide HIV therapy: clinical impact and cost-effectiveness. Ann Intern Med 2001 Mar 20; 134 (6): 440-50

212. Goldie SJ, Paltiel AD, Weinstein MC et al. Projecting the cost-effectiveness of adherence interventions in persons with human immunodeficiency virus infection. Am J Med 2003 Dec 1; 115 (8): 632-41

213. Johri M, Paltiel DA, Goldie SJ et al. State AIDS Drug Assistance Programs: equity and efficiency in an era of rapidly changing treatment standards. Med Care 2002 May; 40 (5): 429-41

214. Freedberg KA, Tosteson AN, Cotton DJ et al. Optimal management strategies for HIV-infected patients who present with cough or dyspnea: a cost-effective analysis. J Gen Intern Med 1992 May-Jun; 7 (3): 261-72

215. Bennett CL, Oddone E, Matchar D. Cost-effectiveness models of clinical trials of new pharmaceuticals for AIDS-related Pneumocystis carinii pneumonia: are they helpful to policy makers? Clin Perform Qual Health Care 1995 Jul; 3 (3): 156-164

216. Wachter RM, Luce JM, Safrin S. Cost and outcome of intensive care for patients with AIDS, Pneumocystis carinii pneumonia, and severe respiratory failure. JAMA 1995; 273: 230-235

217. Bennett CL, Golub RM, Stinson TJ et al. Cost-effectiveness analysis comparing liposomal anthracyclines in the treatment of AIDS-related Kaposi's sarcoma. J Acquir Immune Defic Syndr Hum Retrovirol 1998 Aug 15; 18 (5): 460-5

218. Rachlis A. Incremental cost-effectiveness analysis of intravenous ganciclovir versus oral ganciclovir in the maintenance treatment of newly diagnosed cytomegalovirus retinitis in patients with AIDS. Pharmacoeconomics 1999 Jul; 16 (1): 71-84

219. Castellano AR, Nettleman MD. Cost and benefit of secondary prophylaxis for Pneumocystis carinii pneumonia. JAMA 1991 Aug 14; 266 (6): 820-4

220. Freedberg KA, Tosteson AN, Cohen CJ et al. Primary prophylaxis for Pneumocystis carinii pneumonia in HIV-infected people with CD4 counts below 200/mm3: a cost-effectiveness analysis. J Acquir Immune Defic Syndr 1991; 4 (5): 521-31

221. Freedberg KA, Hardy WD, Holzman RS. Validating literature-based models with direct clinical trial results: the cost-effectiveness of secondary prophylaxis for PCP in AIDS patients. Med Decis Making 1996 Jan; 16 (1): 29-35

222. Goldie SJ, Kaplan JE, Losina E. Prophylaxis for Human Immunodeficiency Virus–Related Pneumocystis carinii Pneumonia: Using Simulation Modeling to Inform Clinical Guidelines. Arch Intern Med 2002; 162: 921-928

223. Bayoumi AM, Redelmeier DA. Preventing Mycobacterium avium complex in patients who are using protease inhibitors: a cost-effectiveness analysis. AIDS 1998 Aug 20; 12 (12): 1503-12

224. Freedberg KA, Cohen CJ, Barber TW. Prophylaxis for disseminated Mycobacterium avium complex (MAC) infection in patients with AIDS: a cost-effectiveness analysis. J Acquir Immune Defic Syndr Hum Retrovirol 1997 Aug 1; 15 (4): 275-282

225. Moore RD, Chaisson RE. Cost-Effectiveness of Prophylaxis for Mycobacterium avium Complex Disease. Am J Med 1997 May 26; 102 (5 Suppl. C): 50-55

226. Sendi PP, Craig BA, Meier G et al. on behalf of the Swiss Cohort Study. Cost-effectiveness of azithromycin for preventing Mycobacterium avium complex infection in HIV-positive patients in the era of highly active antiretroviral therapy. J Antimicrob Chemother 1999 Dec; 44 (6): 811-7

227. Scharfstein JA, Paltiel AD, Weinstein MC et al. The cost-effectiveness of fluconazole prophylaxis against primary systemic fungal infections in AIDS patients. Med Decis Making 1997 Oct; 17 (4): 373-81

228. Moore RD, Chaisson RE. Cost-utility analysis of prophylactic treatment with oral ganciclovir for cytomegalovirus retinitis. J Acquir Immune Defic Syndr Hum Retrovirol 1997 Sep 1; 16 (1): 15-21

229. Paltiel AD, Freedberg KA. The Cost Effectiveness of Preventing Cytomegalovirus Disease in AIDS Patients. Interfaces 1998; 28 (3): 34-51

230. Paltiel AD, Scharfstein JA, Seage GR 3rd et al. A Monte Carlo simulation of advanced HIV disease: application to prevention of CMV infection. Med Decis Making 1998 Apr-Jun; 18 (2 Suppl.): S93-105

231. Paltiel AD, Goldie SJ, Losina E et al. Preevaluation of clinical trial data: the case of preemptive cytomegalovirus therapy in patients with human immunodeficiency virus. Clin Infect Dis 2001 Mar 1; 32 (5): 783-93

232. Rose DN, Sacks HS, Lan V. Cost-effectiveness of cytomegalovirus (CMV) disease prevention in patients with AIDS: oral ganciclovir and CMV polymerase chain reaction testing. AIDS 1997 Jun; 11 (7): 883-7

233. Scharfstein JA, Paltiel AD, Freedberg KA. The cost-effectiveness of prophylaxis for Mycobacterium avium complex in AIDS. Int J Technol Assess Health Care 1999; 15 (3): 531-47

234. Goldie SJ, Kuntz KM, Weinstein MC et al. The clinical effectiveness and cost-effectiveness of screening for anal squamous intraepithelial lesions in homosexual and bisexual HIV-positive men. JAMA 1999 May 19; 281 (19): 1822-9

235. Goldie SJ, Weinstein MC, Kuntz KM et al. The costs, clinical benefits, and cost-effectiveness of screening for cervical cancer in HIV-infected women. Ann Intern Med 1999 Jan 19; 130 (2): 97-107

236. Marra CA, Patrick DM, Marra F. A cost-effectiveness analysis of pneumococcal vaccination in street-involved, HIV-infected patients. Can J Public Health 2000 Sep-Oct; 91 (5): 334-9

237. Rose DN. Short-course prophylaxis against tuberculosis in HIV-infected persons. A decision and cost-effectiveness analysis. Ann Intern Med 1998 Nov 15; 129 (10): 779-86

238. Bell JC, Rose DN, Sacks HS. Tuberculosis preventive therapy for HIV-infected people in sub-Saharan Africa is cost-effective. AIDS 1999 Aug 20; 13 (12): 1549-56

239. Freedberg KA, Scharfstein JA, Seage GR 3rd et al. The cost-effectiveness of preventing AIDS-related opportunistic infections. JAMA 1998 Jan 14; 279 (2): 130-6

240. Yazdanpanah Y, Goldie SJ, Paltiel AD et al. Prevention of human immunodeficiency virus-related opportunistic infections in France: a cost-effectiveness analysis. Clin Infect Dis 2003 Jan 1; 36 (1): 86-96

241. Moore AR, Wiffen PJ, Lipsky BA. Are the pneumococcal polysaccharide vaccines effective: meta-analysis of the prospective trials. BMC Family Practice 2000; 1(1)

242. Pérez-Casas C. HIV/AIDS medicines pricing report: Setting objectives, is there a political will? Médecins Sans Frontières. 2000 [online]. Available from URL: http://www.accessmed-msf.org/prod/publications.asp?scntid=492001113146&contenttype=PARA& [Accessed 2005 Feb 5]

243. Médecins Sans Frontières. AIDS drugs now available for 36 cents a day under Clinton Foundation deal [online]. Available from URL: http://www.accessmed-msf.org/prod/publications.asp?scntid=23102003162679&contenttype=PARA& [Accessed 2005 Feb 5]

244. Edejer TT. Disseminating health information in developing countries: the role of the internet. Br Med J 2000; 321: 797-800

245. Khan MA, Walley JD, Witter SN et al. Costs and Cost-effectiveness of different DOT strategies for the treatment of tuberculosis in Pakistan. Health Policy Plann 2002; 17 (2): 178-86

246. Farmer P, Léandre F, Mukherjee JS et al. Community-based approaches to HIV treatment in resource-poor settings. Lancet 2001; 358: 404-9

247. Liechty CA, Bangsberg DR. Doubts about DOT: antiretroviral therapy for resource-poor countries. AIDS 2003 Jun 13; 17(9): 1383-7

248. World Bank. Project Appraisal Document on a proposed credit in the amount of SDR 140.82 to India for a Second National HIV/AIDS Control Project. Health, Nutrition and Population Sector Unit, South Asia region. 1999 May 13. World Bank report No. 18918-IN

249. Joint United Nations Programme on HIV/AIDS (UNAIDS). Innovative Approaches to HIV Prevention, Selected Case Studies. Geneva: UNAIDS. 2000 Oct; Report No. 00.35E

250. Beck EJ, Miners AH, Tolley K. The cost of HIV Treatment and Care: A Global Review. Pharmacoeconomics 2001; 19 (1): 13-39

251. Berk ML, Maffeo C, Schur CL. Research Design and Analysis Objectives. AIDS Cost and Services Utilization Survey (ACSUS) Reports, No. 1. Rockville, MD: Agency for Health Care Policy and Research. 1993; AHCPR Publication No. 93-0019

252. Beck EJ, Mandalia S, Gaudreault M et al. The Cost-effectiveness of HAART, Canada 1991-2001. AIDS 2004; 18: 2411-9

253. Marseille E, Hofmann PB, Kahn JG. HIV prevention before HAART in sub-Saharan Africa. Lancet 2002; 359: 1851-6

254. Médecins Sans Frontières. AIDS Triple Therapy for Less than $1 a Day [online]. Available from URL: http://www.accessmed-msf.org/prod/publications.asp?scntid=2182001328382&contenttype=PARA& [Accessed 2005 Feb 5]

255. Beck EJ, French PD, Helbert MH et al. Improved Outcome of Pneumocystis Carinii Pneumonia in AIDS Patients: a multifactorial treatment effect. Int J STD AIDS 1992; 3: 182-7

256. World Health Organisation. HIV Patient ART Monitoring Meeting: International Conference Centre, Geneva, 29-31 March 2004 and Beyond [online]. Available from URL: http://www.who.int/3by5/publications/documents/artmonitoring/en/ [Accessed 2005 Feb 5]

257. Beaglehole R, Bonita R. Public Health at the Crossroads: achievements and prospects. Cambridge: Cambridge University Press. 1997: 124-5

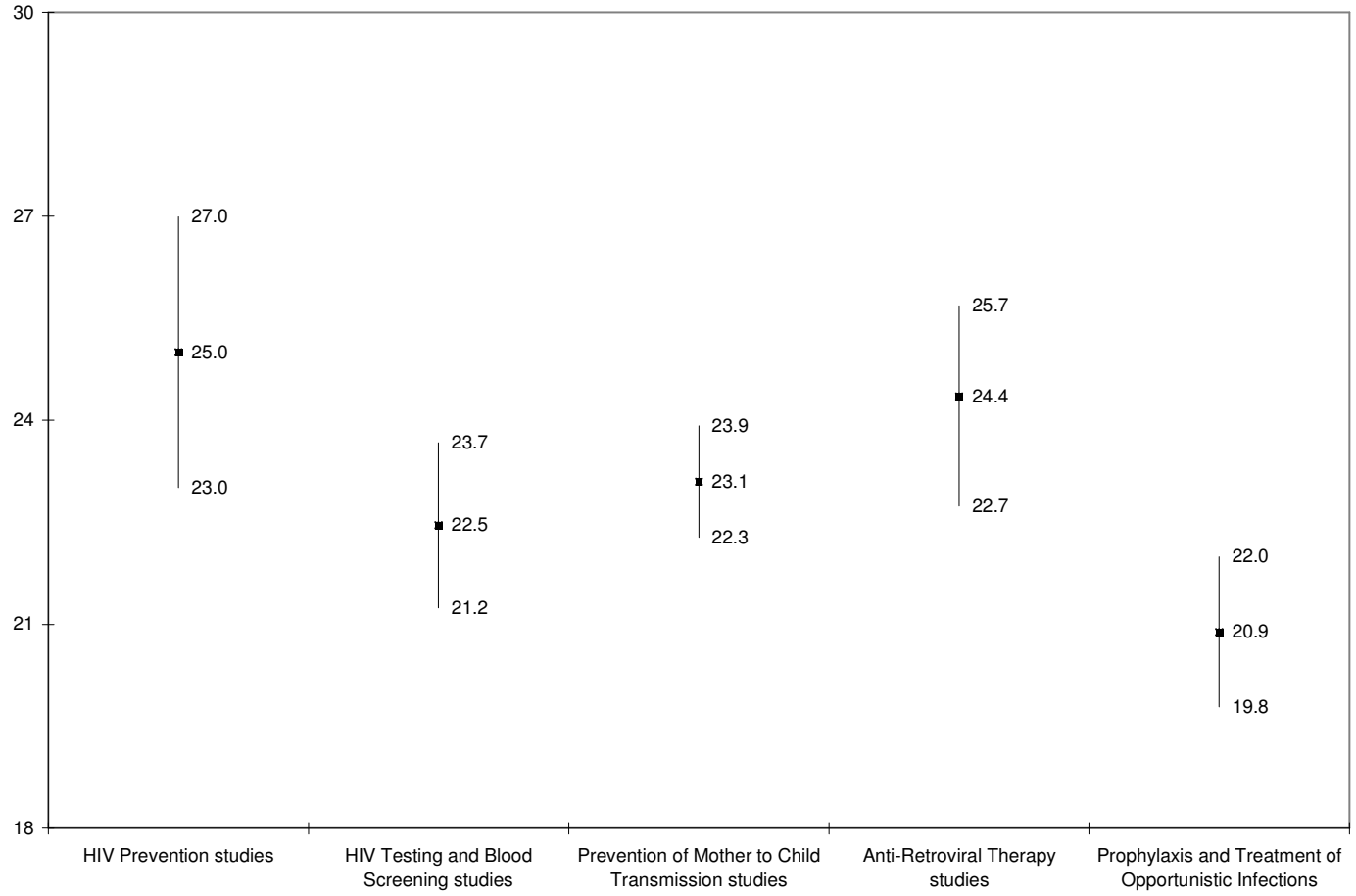

Figure 1: Mean score and 95% confidence interval for the five study categories.