Cost-Effectiveness of Using HAART in Prevention of Mother-To-Child Transmission in the DREAM-Project Malawi

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Introduction: Cost-effectiveness analysis are crucial in the management of the HIV/AIDS epidemic, particularly in resource-limited settings. Such analyses have not been performed in the use of highly active antiretroviral therapy (HAART) for prevention of mother-to-child transmission (PMTCT).

Objective: Cost-effectiveness analysis of HAART approach in Malawi for PMTCT.

Methods: In 2 health centres in Malawi 6500 pregnant women were tested; 1118 pregnant women completed the entire Drug Resource Enhancement against Aids and Malnutrition–Project Malawi (DREAM - PM) PMTCT protocol. The costs of the intervention were calculated using the ingredients method. Outcomes estimated were cost for infection averted and cost for DALY saved compared with no intervention.

Results: From a private perspective cost for HIV infection averted was US $998 and cost per DALY saved was US $35.36. From a public perspective, the result became negative as follows: −261 and −16.55, respectively (lower cost than the cost of the therapy for an HIV+ child). The univariate sensitivity analysis showed that the cost for DALY saved always remained under the threshold of US $50, largely under the threshold given by the per capita yearly income in Malawi (US $667 PPD).

Conclusions: Administration of HAART in a PMTCT programme in resource-limited settings is cost-effective. Drugs and laboratory tests are the most significant costs, but further reduction of these expenses is possible.

Key Words: cost-effectiveness, DREAM, HAART, mother-to-child-transmission, Malawi

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INTRODUCTION

There are several protocols in use worldwide for prevention of mother-to-child HIV transmission, and they have varying degrees of efficacy. These differ from each other in terms of the type of drugs administered, the complexity of the regimen, and duration of administration. Each protocol, therefore, has its own cost and a specific level of effectiveness. Great emphasis is currently being given to the economic evaluation of HIV control policies and interventions in developing countries. Some recent studies have supplied information on the cost-effectiveness of many prevention of mother-to-child transmission (PMTCT) approaches, but there is still no complete analysis of protocols based on highly active antiretroviral therapy (HAART). This protocol is now recommended by the WHO as a possible option for PMTCT even in resources-limited settings.[1]

The aim of this study was to conduct an assessment of the cost-effectiveness of a HAART-based intervention: Drug Resource Enhancement against Aids and Malnutrition (DREAM) in PMTCT compared with a no intervention scenario. The intervention included voluntary counselling and testing and adopted a holistic approach combining HAART (3TC-ZDV/D4T-NVP), irrespectively of the patients' immunological status from the 25th week of pregnancy, with the treatment of malnutrition, tuberculosis, malaria, and sexually transmitted diseases.[2] HAART was also administered during breastfeeding (BF) until 6 months after delivery, if the women adequately counselled chose to breastfeed. Whether the baby was breastfed or not the protocol is completed upon infant weaning (6th month), which terminates the risk of exposure to HIV transmission.

METHODS

We assessed the cost-effectiveness of a PMTCT program implemented at DREAM-PM centres in Malawi: Blantyre, and Mtemgowamtemga (Lilongwe).

During 42 months of activity (from July 2005 to December 2008), 6500 women received counselling during their antenatal care (ANC) visits; 5467accepted testing, 1371 tested HIV positive, and 1206 joined the program. Of these, 1118 completed the entire PMTCT protocol.

Costs

For the cost analysis, all expenses borne by the DREAM-PM program throughout 42 months of intervention at the 2 centres in Blantyre and Lilongwe were aggregated

through the ingredients method. The information on costs was extracted from the accountability records of the DREAM-PM program and from data on the program activities registered in the software of the monitoring and evaluation program.

The cost of drugs was calculated according to the average cost for 1 year of therapy in Malawi in 2007 USD and amounted to US $204 per year (commercial prices on the market for first-line therapy generic drugs). The average duration of therapy for women enrolled in the program was estimated to be 10 months.

Because voluntary testing and counseling (VCT) generates benefits beyond its role in the reduction of mother-to-child transmission (MTCT), the costs of VCT should be deducted from PMTCT program costs. Because VCT can reduce horizontal HIV transmission and is often funded exclusively for this purpose, a significant portion of MTCT-related costs can be attributed to these other (non-MTCT) benefits. In the absence of data estimating the extent of this additional benefit, the model incorporated a discount amounting to 15% for VCT in the base case, as has previously been done in similar studies.[3] The impact of varying the value of this estimate between 0% and 30% was considered in the sensitivity analysis.

The analysis was undertaken from a private perspective, namely taking into account the costs borne by the service provider and from a public perspective. The public perspective takes into account the costs borne by the local public health service and cost savings to the public sector given the number of infections averted.

Several studies have tried to estimate the discounted life-time HIV-related health care costs for infants with HIV in sub-Saharan Africa, with a large spectrum of results depending on various factors like the area of the intervention, the level of the country's health expenditure, the urban/rural environment, etc. In the United States, a life-time discounted cost of $113,476 is calculated for 9 years of survival, $151,849 for 15 years, and $228,155 for 25 years.[4] Studies carried out at the end of the 1990s estimated a life-time discounted cost in sub-Saharan countries of $281–$517.[3,5] Other studies estimated higher costs, for an annual cost of $380,[6] which would amount to around $2017, bearing in mind the progression of the disease reported later on in the study (All values of citated studies in this section are reported in US dollars as of 2007 and adjusted from prior years using the medical services component of the consumer price index (www.bls.gov/cpi/home.htm). Nonetheless those estimates were performed during a period in which there was only a minimal use of paediatric HAART. More relevant studies in South Africa indicate a life-time discounted cost of $2497 in a situation in which HAART is not available and $10,969 where HAART is available.[7]

In the present study, as far as therapy is concerned, the authors have attempted a pragmatic approach based on the DREAM-PM experience in 7 years of activity, with a cohort of approximately 6000 children. On this basis, an annual cost of paediatric HAART of $195 (10% of children needs pediatric syrup with an average annual cost of US $950, whereas the remaining 90% can use the formulation in tablet with an average annual cost of US $108) has been calculated for first-line therapy and $950 for second-line therapy. Later Soorapanth et al[7] considered a unit cost of $426 for the hospitalization of children.

The progression of HIV and AIDS considered is the one estimated by Chin[8] and already used in similar studies: 25% of cases manifest 1 year with HIV and 1 year with AIDS before dying; 55% of cases 5 years with HIV and 1 year with AIDS before dying; and the remaining 20% 10 years with HIV and 1 year with AIDS before dying.

On this basis, one can calculate a mean discounted life-time cost of $1259 per child including the cost of hospitalization, diagnostic and antiretroviral therapy (first line).

For the purposes of the analysis, all prices were converted to US $2007 using the medical services component of the consumer price index, and expenses in local currency were converted according to the daily exchange rate at the time the expense was made. All costs borne by the program that were not relevant to the PMTCT service were excluded from the calculation of costs. A 3% discount rate on annualized fixed costs was applied (6% and 0% used in the sensitivity analysis).

Analysis of Effectiveness

The MTCT rate in PACTG 076 was 25% without BF.[9] BF poses an additional 14%–16%, based on meta-analysis studies. Thus most people consider an overall 40% risk. In the present study, the conservative value of 35.9%[3] has been considered, to make the comparison of the results with similar studies easier.

The indicators used to evaluate the effectiveness of the intervention were the number of infections averted and DALY saved compared with a nonintervention scenario. The reduction of the risk of transmission compared with non-intervention was considered as an intermediate indicator of effectiveness.

The net number of DALY generated by an averted infection was a function of the difference between the expected number of quality-adjusted life-years (QALY) of HIV-positive children and the expected number of QALY of HIV-negative children,[10] assuming life expectancy at birth without AIDS to be 56.7 years.[11] Murray and Lopez[12] weights of 0.123 for HIV and 0.505 for AIDS were used to make the disability adjustments.

QALY were further adjusted by age–weight to reflect the variation in the social value of life-years as a function of age. We used a standard age–weight function based on expert consensus and employed by the World Bank.[13] We also used a discount rate for future benefits of 3% normally considered in cost-effectiveness analysis. All these parameters have been considered in the sensitivity analysis.

RESULTS

Costs

Analyzing DREAM-PM expenditures over 42 months of activities resulted in the costs shown in Table 1.

Listed in the first column are the annual costs of the investments discounted for services other than PMTCT. The second column lists average costs per patient for the entire treatment period. The third column lists the discounted total

TABLE 1. DREAM-PM Programme Costs

	Annual Costs	Cost per Pregnant Patient in the PMTCT Program*	Cost for 6500 Women of Programme (42 Months)†
Variable costs			
Staff		$64	$75,249
Rapid test		$2	$2585
Lab examinations		$70	$82,346
Drugs		$170	$199,476
Total		$306	$359,657
Fixed costs			
Facilities	$17,585	$40	$49,740
Car	$5275	$12	$14,922
Furniture/pc	$3658	$8	$10,348
Total		$60	$75,010
Grand total		$366	$434,666

*From 25th week prepartum to 6 months postpartum.
†Net present value with 3% discount for future costs.

cost for 6500 women included in the program in 42 months of intervention, taking into account the 3% discount rate on future costs. The total cost of US $434,666 for 6500 women is equal to US $67 per woman tested and US $366 per woman entered in the PMTCT protocol with HAART.

The most important entries are laboratory tests and drugs, but these costs have decreased substantially since the programme was launched in 2001. This is because as the services of DREAM-PM developed, the large dimensions of the program allowed for the reduction of costs thanks to economies of scale.

The use of HAART for PMTCT purposes was responsible for reduction in maternal virus load with a very low cumulative transmission rate at 12 months of 2.8%.[14] Thus the effectiveness of the DREAM approach has shown a 75.24% reduction of risk including loss to follow-up or patient refusal, which translates into 370 infections averted in our cohort compared with no intervention. This generates a total of 10,449 DALY saved.

Final results of the Cost-effectiveness analysis are shown in Table 2 according to the different levels of analysis as follows: (1) private perspective, (2) public perspective.

Univariate sensitivity analysis was conducted on the main epidemiological and economic variables. The transmission rate was set at 5.6%, the double of base case (2.8%) and at 0%. The risk reduction rate was set at 15% more and less of the base case. The average prevalence in Malawi is 11.9% and was a little higher in 2005 among pregnant women (median value of 18.6% in urban areas and 14.6% in rural area),[15] but in our cohort, 25.07% tested positive. The higher value is likely due the fact that the woman who had the probability to be infected was more predisposed to undergo VCT during pregnancy. In the sensitivity analysis, the value of 10% and 40% for prevalence rate was considered.

Regarding economic variables, the cost of lab exams and drugs was set to ±20% of the original value, the interest rate was set at 0% and 6%, the discount for external benefit was set to 0% and 30%, and the HIV+ child's life-time cost was set at ±50% of the original value.

The results of the analysis are reported in Table 3. The cost for DALY saved always remained under the threshold of US $50 to be considered cost-effective. It also remained largely under the threshold given by the per capita yearly income in Malawi of US $667 purchasing power parity. To evaluate the possibility of implementation of this approach in other settings, the program remained cost-effective (less than US $50 per DALY saved) from a private (public) perspective with a reduction of the risk of transmission higher than 53.20% (28.12%), with a prevalence rate more than 8.5% (2.83%) and with a total cost per woman tested less than US $95 (US $179). From the public perspective, the cost per DALY saved is equal to 0 if the mean life-time cost for the treatment of an HIV+ child is equal to US $370.

TABLE 2. Cost-effectiveness Analysis Results

Perspective	Private	Public
Total cost for 6500 women (discounted)	$369,466	(−$96,748)
HIV-1 cases averted	370	370
DALYs saved	10,449	10,449
Cost per infection averted	$998	(−$261)
Cost per DALY saved	$35.36	(−$16.55)

CONCLUSIONS

In conclusion, it is possible to affirm that the administration of HAART to pregnant women in a PMTCT program in a resource-limited setting is cost-effective.

Success rates are reinforced if the program reaches good levels of patient retention and an efficient use of available resources.

The costs of drugs and laboratory tests remain the most significant cost to the program, but a further reduction of these costs is possible with scaling up, and this greatly enhances the program's cost-effectiveness.

Other external benefits of administration of HAART were not assessed in this study, such as the reduction of the number of orphans by the prolongation of maternal life expectancy, which also leads to a reduction in public health expenditures; the investment in human capital through the training of skilled personnel, such as laboratory technicians, clinical officers, counsellors, pharmacy and nutritional experts, which positively affect the entire health sector; the reduction of stigma due to improved quality of life enjoyed by HIV+ mothers undergoing treatment; and the decline of horizontal transmission of virus by the use of HAART and the improvement of health care in general in resource-limited settings. All of these parameters should be taken into consideration in future studies.

It is worth to note that the cost-effectiveness of this approach is a confirmation of the economic feasibility and sustainability of the similar approach recommended as option B by the WHO 2010 guidelines.[1] Nevertheless the high cost of this intervention means that this is not affordable for many less developed countries. International aid is therefore necessary to

TABLE 3. Univariate Sensitivity Analysis

Perspective	Cost Per Infection Averted (US $)		Cost Per DALY Saved (US $)	
	Private	Public	Private	Public
Base case results	998	−261	35	−9
Transmission rate (0%–5.6%)	920–1090	−339 to −169	32.6–38.63	−12.02 to −5.99
Reduction of risk (60%–90%)	1251–834	−8 to −425	44.34–29.56	−0.28 to −15.06
Prevalence rate (10%–40%)	1319–919	59 to −341	46.72–32.54	2.1 to −12.07
Exams cost (−20% to +20%)	960–1036	−299 to −224	34.02–36.7	−10.6 to −7.92
ARV drugs cost (−20% to +20%)	906–1090	−353 to −170	32.11–38.6	−12.5 to −6.01
Interest rate (0%–6%)	1038–963	−363 to −179	36.76–34.12	−12.87 to −6.35
Discount for external benefits (0%–30%)	1174–822	−85 to −437	41.6–29.12	−3.02 to −15.5
HIV+ children treatment life-time cost (−50% to +50%)	—	368 to −891	—	13.05 to −31.57

sustain and enforce the fight against the HIV/AIDS pandemic to make effective interventions possible.

An interesting economic analysis to be performed in the near future would be the comparison of the current approach discussed herein with other protocols for PMTCT as for instance option A of the WHO 2010 guidelines.[1]

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