Cost-Effectiveness and Quality of Care of a Comprehensive ART Program in Malawi

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Abstract: The aim of this study is to assess the cost-effectiveness of a holistic, comprehensive human immunodeficiency virus (HIV) treatment Program in Malawi.

Comprehensive cost data for the year 2010 have been collected at 30 facilities from the public network of health centers providing antiretroviral treatment (ART) throughout the country, two of these facilities were operated by the Disease Relief through Excellent and Advanced Means (DREAM) program.

The outcomes analysis was carried out over five years comparing two cohorts of patients on treatment: 1) 2387 patients who started ART in the two DREAM centers during 2008, 2) patients who started ART in Malawi in the same year under the Ministry of Health program.

Assuming the 2010 cost as constant over the five years the cost-effectiveness analysis was undertaken from a health sector and national perspective; a sensitivity analysis included two hypothesis of ART impact on patients’ income.

The total cost per patient per year (PPP Y) was $314.5 for the DREAM protocol and $188.8 for the other Malawi ART sites, with 737 disability adjusted life years (DALY) saved among the DREAM program patients compared with the others.

The incremental Cost-Effectiveness Ratio was $1640 per DALY saved; it ranged between $896–1268 for national and health sector perspective respectively. The cost per DALY saved remained under $2154 that is the AFR-E-WHO threshold.

HIV/acquired immune deficiency syndrome comprehensive treatment program that joins ART with laboratory monitoring, treatment adherence reinforcing and Malnutrition control can be very cost-effective in the sub-Saharan African setting.

INTRODUCTION

The world has made significant progress in scaling up human immunodeficiency virus (HIV) treatment. There were 13.9 million HIV positive patients receiving antiretroviral therapy (ART) in sub-Saharan Africa at the end of 2013. In Malawi the number of patients alive on ART reached the number of 472,865 at the end of December 2013. ART showed to be the game-changer in the HIV epidemic: in Malawi the incidence dropped to 0.4 per 100 person-years, the lowest from the beginning of epidemic. However, there is still a long way to go to reach the ambitious 90–90–90 strategy released by UNAIDS in 2014. This approach will include a "test and treat" approach, which finally will put on treatment many patients in an early stage of the infection with a positive impact on HIV morbidity and mortality. It is likely that the enormous increase of funds needed to support the increased number of treatment will be cost effective compared with the current guidelines, as showed in the cost-exercise included in the 2015–2020 Malawi National Strategic Plan (NSP).

Over time countries have begun to apply more innovative models of care to ensure better patient outcomes and reduce transmission. There has been significant study of these models. Malawi embraced the ambitious 90–90–90 strategy released by UNAIDS in 2014. This approach will include a deep shift of the national treatment guidelines towards a ‘‘test and treat’’ approach, which finally will put on treatment many patients in an early stage of the infection with a positive impact on HIV morbidity and mortality. It is likely that the enormous increase of funds needed to support the increased number of treatment will be cost effective compared with the current guidelines, as showed in the cost-exercise included in the 2015–2020 Malawi National Strategic Plan (NSP).

The authors report no conflicts of interest.

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MEDICINE
The aim of this study is to assess the cost-effectiveness of a holistic, comprehensive HIV treatment program: The Disease Relief through Excellent and Advanced Means (DREAM) program in Malawi. This program includes ART treatment with extensive laboratory monitoring including regular CD4 cell count and viral load monitoring (biannual and annual respectively). It also includes a program to improve retention and adherence through peer-to-peer education and extensive use of information technology (IT) aimed to allow patients’ tracing in case they gave consent to this intervention. The Balaka DREAM centre provides nutritional supplementation to the patients with Body Mass Index lower than 18.5 and to all children who started ART. Nutritional supplementation is only occasionally provided to patients registered at Namandanje.17

METHODS

The study below compares one year of cost data from 2010 to five years of health outcomes in order to capture a medium to long-term impact of ART on patients’ health and on cost to support for the health sector.

The cost analysis presented in this paper draws from a larger dataset gathered and analysed in the framework of the Multi-Country Analysis of Treatment Costs for HIV/AIDS (MATCH) study carried out by the Clinton Health Access Initiative, in collaboration with the Governments of Ethiopia, Malawi, Rwanda, South Africa and Zambia and the Centre for Global Development. This study was conducted in 161 facilities across the five countries in order to analyse cost of ART provision.18

In Malawi, comprehensive cost data for one year of facility-level ART in 2010 was collected at 30 facilities from the public network of health centres providing ART throughout the country.1 The data collection methodology and calculation of cost-per-patient-years have been already described in a previous publication.18 Additional patient data from the DREAM database on date of ART initiation, time on treatment, and visit intensity were used to determine the number of patient years for new and established patients at the two DREAM facilities. Using the methods described in the MATCH methodology to collect the empirical cost and patient data as well as additional patient data from the DREAM database, the cost for new and established patients at the DREAM facilities was calculated through the same allocation and derivation per cost per patient year described in the MATCH paper.

Of the 30 sites that were randomly selected, the DREAM program operated two sites. The two DREAM sites (Balaka and Namandanje) are managed by the Community of Sant’Egidio and provide free-of-charge antiretroviral (ARV) care to people living with HIV/AIDS through the administration of ARV drugs provided by the government and according to the regimens established by the Malawian Guidelines. At the time of the MATCH study, the Malawi National Guidelines ART initiation criteria included those at WHO (World Health Organization) clinical stage 3–4 or with a CD4 count lower than 250 cells/μL. Since 2010 ART has been offered to all patients at stage 3–4 and CD4 count lower than 350 cells/μL.

The outcomes analysis was conducted over five years and focuses on patients with baseline CD4 count lower than 250 in order to make the sample comparable to the patients who accessed ART during the cost data year (2010). The analysis compared two cohorts of patients on treatment over that time period. The first cohort was made up of all the patients who started ART in the two DREAM centres during 2008 using data from the DREAM Electronic Medical Records system. The second cohort included patients who started ART in Malawi from April 1st to June 30th, 2008 under the Ministry of Health program (MOH, Malawi, 2008 and 2013) using data from the Ministry of Health quarterly report.19

The Malawi National program statistics on survival and retention in care after five years were applied to both cohorts in order to generate the number of averted deaths and the number of disability adjusted life years (DALY) saved.20 Murray and Lopez weights of 0.505 for AIDS were used to make the disability adjustments.21 We used a standard age–weight function based on that employed by the World Bank.22

For the purpose of performing comparison with the World Health Organization cost-effectiveness threshold of intervention, costs were also calculated according to the average cost for one year of in Malawi in 2010 USD purchasing power parity (PPP). Expenses incurred in local currency (salaries, equipment and administrative services, patient support) have been adjusted to international USD (PPP) using a 2010 World Bank PPP conversion factor23 and June 2010 USD/MWK exchange rate.24

The analysis was undertaken from a health sector perspective, namely taking into account the costs borne by the service provider or third parties like international donors (e.g., drugs bought by the Global Fund). This was complemented with an analysis conducted under the national perspective with the hypothesis that ART has a direct impact on patients’ income, thus generating a net increment in gross domestic product (GDP) of the country. According to international literature, sustained ART can double per capital income through improved employment opportunities and productivity in 6 months time.25–28 Therefore it was assumed that pre-therapy average income for future patients was 50% of the average per capita income of Malawi ($722),29 that in six month time it will double in order to reach the pre-AIDS status. A low-estimate of this increment (+50%) has been considered as a most conservative scenario. To consider the gradualism of the effect over the time in the first 6 months the increment has been reduced of the half. The net increase in income was therefore considered to offset the total cost of the program.

A 3% discount rate on annualised fixed costs and on future gains was applied. We also used a discount rate for future benefits of 3% normally considered in cost-effectiveness analysis.

A sensitivity analysis has been conducted on the following variables: interest rate (0%–6%); difference of cost per person between the two cohorts (−30% – +30%); PPP conversion rate (−15% – +15%); DREAM patients survival rate (−5% – +5% on each year). The survival and retention in care rate, in both scenarios, considered lost-to follow-up (LTFU) also those patients who are still in care but have been transferred to other centres. We assumed the number of transferred is proportional in the two scenarios, not affecting the cost-effectiveness comparison. However in the sensitivity analysis we also considered the possibility of an higher mobility in the government centre, reducing the difference between survival and retention in care in the two approaches of 15%.

Descriptive analysis was performed in STATA IC13 and Microsoft Excel 2007 to calculate ART costs per patient per year (PPPY). Outcome data analysis, including descriptive analysis and survival analysis, was performed with SPSS 19.0 package.

It was not required the approval of an ethics committee, as the present study is based solely on epidemiological data published by the government of Malawi and economic values. As regards the data on the survival and virological status of
patients enrolled in DREAM centres they are routinely collected as prescribed by national protocols.

RESULTS

The average facility-level cost of treatment PPPY was found to be $188.8, 321.1 and 298.4 at the National average, Balaka DREAM and Namandanje DREAM sites respectively (Table 1). On average the DREAM model costs were 66.5% higher than government ART sites.

Across all facilities in the MATCH study, ARVs accounted for the bulk of all costs, followed by personnel. Higher costs for the DREAM model were came from 3 key areas, which accounted for 90% of the cost difference: personnel, ARVs and laboratory services (details in Table 2). Salaries accounted for 55.3% of the entire cost variation or $69.5 per person per year. The difference was due in part to variation in staffing levels, staffing mix and salary levels. Balaka Dream and Namandanje Dream both had higher number of staff per 1,000 patients, and particularly more laboratory and pharmaceutical technicians (Table 3). They also had higher average salary levels. ARVs accounted for 13.8% ($17.4) of the cost variation due in part to the procurement of ARVs for advanced stage patients with resistance to many government-procured ARVs. Finally, laboratory testing was performed more frequently at DREAM sites, accounting for 20.5% ($25.7) of the cost variation.

In order to capture a long term impact on survival of the two approaches a comparison of being alive and on care rates has been carried out (Table 3). The two cohorts showed comparable composition in terms of gender (65.6% and 63% of females for the DREAM and government cohort respectively) and age (15.6% and 9% of children respectively). The alive and being on care rate is quite similar among adult and children in both cohorts (data not showed) Table 4 shows a cumulative increase of survival and being on care rate of 33% (79.8% vs 60%) that translates into 737 DALY saved; the increase is more evident at the end of the first year of care mainly due to the better immunological and clinical condition of many patient at baseline assessment due to the routine use of CD4 count and the increased CD4 count threshold to start ART.

Based on the total cost PPPY of $314.5 for the DREAM protocol and $188.8 for the other Malawi ART sites, the total net present value of incremental cost in the DREAM protocol for the cohort of 2,387 patients has been estimated in $1,208,345 for the 5-year period (Table 4). Given the Malawi annual GDP per capita of 722 USD PPP, we assumed the pre-ART baseline patients income as half of the National per-capita GDP and the income increment of $361–180.5 (high estimate and low estimate respectively). Accordingly, the total discount applied in the national perspective is $548,523 to $274,262.

TABLE 1. Cost of Treatment per Patient Year

|                | Malawi (Average) | Balaka (Dream) | Namandanje (Dream) | DREAM (Weighted Average) |
|----------------|------------------|----------------|---------------------|-------------------------|
|                | USD | PPP  | USD | PPP  | USD | PPP  | USD | PPP  | USD | PPP  |
| ARVs Mean      | 66.0| 66.0 | 86.0| 86.0 | 77.0| 77.0 | 83.4| 83.4 |
| %              | 48.5| 35.0 | 37.7| 26.8 | 36.5| 25.8 | 37.4| 26.5 |
| Non-ARVs Mean  | 10.0| 10.0 | 16.0| 16.0 | 8.0 | 8.0  | 13.7| 13.7 |
| %              | 7.4 | 5.3  | 7.0 | 5.0  | 3.8 | 2.7  | 6.1 | 4.3  |
| Staff Mean     | 29.0| 56.8 | 63.0| 123.5| 68.0| 133.3| 64.4| 126.3|
| %              | 21.3| 30.1 | 27.6| 38.5 | 32.2| 44.7 | 28.9| 40.2 |
| Lab costs Mean | 4.5 | 4.5  | 29.0| 29.0 | 35.0| 35.0 | 30.7| 30.7 |
| %              | 3.7 | 2.6  | 12.7| 9.0  | 16.6| 11.7 | 13.8| 9.8  |
| Other costs†   | 26.0| 51.0 | 34.0| 66.6 | 23.0| 45.1 | 30.8| 60.4 |
| %              | 19.1| 27.0 | 14.9| 20.8 | 10.9| 15.1 | 13.8| 19.2 |
| Total          | 136.0| 188.8| 228.0| 321.1| 211.0| 298.4| 223.1| 314.5|
|                | 100.0| 100.0| 100.0| 100.0| 100.0| 100.0| 100.0| 100.0|

ARV = antiretroviral, DREAM = Disease Relief through Excellent and Advanced Means, PPP = purchasing power parity, USD = US dollar.
†Nutritional support, facility-level training, equipment, clinical and nonclinical supplies, building maintenance, other administrative support costs.

TABLE 2. Average Lab Cost and Frequency

| Facility ID       | Laboratory Cost PPPY | CD4 Tests PPPY | VL Tests PPPY | FBC Tests PPPY |
|-------------------|----------------------|----------------|---------------|----------------|
| Malawi (average)  | $4.54                | 0.2            | 0.1           | 0.2            |
| Balaka dream      | $28.71               | 1.2            | 0.7           | 1.8            |
| Namandanje dream  | $35.44               | 1.4            | 0.9           | 1.1            |

FBC = full blood count, PPPY = per person per year, VL = viral load.
Taking the cost and impact data together, the incremental cost-effectiveness ratio (ICER) of the intervention is calculated as $1,640 per DALY saved from the health sector perspective and $896 – 1268 from the national perspective (Table 5). The cost per DALY saved remained under the threshold of GDP per capita of AFR E WHO Region of 2154 USD PPP and can therefore be considered very cost-effective according to WHO standards,30 in case the Malawi GDP is considered (722 USD PPP) the cost per DALY saved remains under the threshold of three times the GDP value that is 2166 USD PPP so that it must be considered very cost-effective as per the WHO classification.

The sensitivity analysis is reported in Table 6. The most relevant variable is the survival and retention in care rate in the DREAM cohort. Reducing this rate of 5% each year produce an ICER cost from the health sector perspective of $2212, exceeding the threshold to be very cost-effective. This confirms the importance of the effectiveness side of the analysis, and the importance of monitoring closely this factor to produce solid results.

**DISCUSSION**

Cost analysis of HIV/AIDS program reported in literature usually are not as detailed as this analysis or based on shorter follow up periods or on prospective analysis modelled on mathematical simulation rather than real data.8–10,12–15 The mathematical simulation rather than real data.8–10,12–15 The follow up periods or on prospective analysis modelled on usually are not as detailed as this analysis or are based on shorter standards;30 in case the Malawi GDP is considered (722 USD PPP) the cost per DALY saved remains under the threshold of three times the GDP value that is 2166 USD PPP so that it must be considered very cost-effective as per the WHO classification.

The cost structure is similar between the DREAM sites and national programs, with the highest expense attributed to ARVs followed by staff (Real Money Value). However, after the PPP conversion, the highest cost became the staff salary for the DREAM program. The personnel to patient ratio, or staffing, is comparable between the two programs though two DREAM sites had a greater number of Laboratory technicians and Pharmacists. Compared to other countries in the MATCH study, the personnel/patients ratio in HIV care is low. It is also low in health care as a whole (WHO 2010). However, the salaries of some cadres were higher for the DREAM program, particularly high-qualified technical staff, partially as results of the requirements of being an international non-governmental organization (NGO). The increasing number of patients due to the recent change of criteria to access ART may require an increase of personnel dedicated to HIV care. It may also be necessary to provide incentives for medical personnel to work in more remote facilities to encourage decentralization. These factors could increase the National Program personnel cost in the future.

Salaries for some cadres were higher for the DREAM program partially as results of specific working relation dynamic involving an international NGO. The National Program allowing further savings can avoid this dynamic. However, the crucial role of the relation between personnel attitude and higher patients’ adherence to treatment must be stressed.

**TABLE 4. Comparison of Survival and on Care Rate and Increase of Program Costs, DALY Saved and Patient’s Income for the DREAM Program vs MW National Program**

| Effectiveness | 1 y | 2 y | 3 y | 4 y | 5 y | Total | Net Present Value 
|---------------|-----|-----|-----|-----|-----|-------|----------------|
| % patients survived DREAM | 89.00 | 85.10 | 83.00 | 81.00 | 79.80 | 79.80 | 79.80 | 79.80 | 79.80 |
| % patients survived MW | 79.00 | 74.00 | 69.00 | 63.00 | 60.00 | 60.00 | 60.00 | 60.00 | 60.00 |
| Number of survived DREAM | 2125 | 2032 | 1982 | 1934 | 1906 | 1906 | 1906 | 1906 | 1906 |
| Number of survived MW | 1887 | 1767 | 1648 | 1504 | 1433 | 1433 | 1433 | 1433 | 1433 |
| Averted death | 239 | 265 | 334 | 430 | 473 | 473 | 473 | 473 | 473 |
| DALY saved | 101 | 112 | 141 | 182 | 200 | 200 | 200 | 200 | 200 |
| Incremental program costs | ($300,230 | $267,205 | $255,496 | $249,191 | $243,186 | $243,186 | $243,186 | $243,186 | $243,186 |
| DALY saved | 101 | 112 | 141 | 182 | 200 | 200 | 200 | 200 | 200 |
| Increased patients income | High estimate | $64,655 | $95,690 | $120,690 | $155,172 | $170,689 | $170,689 | $170,689 | $170,689 |
| Low estimate | $32,328 | $47,845 | $60,345 | $77,586 | $85,345 | $303,448 | $303,448 | $303,448 | $303,448 |

**ART** = antiretroviral treatment, **DALY** = disability adjusted life years, **DREAM** = Disease Relief through Excellent and Advanced Means.

*All DREAM program patients who started ART during 2008, 2387 individuals.

†All Malawian patients who started ART between April and June 2008, about 30,000 patients (Source: Malawi MOH—Integrated HIV Program Report April–June 2013).

‡The cost is the difference between the cost in DREAM protocol of $314.5 and the cost in Malawi of $188.8 by for the number of patient at the beginning of the year (2387).

§The difference from the total is given by the discount rate at 3% on future costs.

ICER = incremental cost-effectiveness ratio.
Laboratory costs have been shown to reduce mortality in a number of studies. Patients with CD4 monitoring performed better than those without CD4 monitoring during the DART trial. Viral load is also critical to quickly detect virological failure and adherence failure and support doctors in patient management. The DREAM program includes both regular CD4 count and regular viral load monitoring tests. These monitoring costs constitute 10% of total HIV expenses. Savings could be generated in this area but moving away from CD4 testing. This would be in line with the new National program guidelines in Malawi, which prioritise viral load over CD4 testing for monitoring. Economies of scale could facilitate the reduction in laboratory reagent costs if adopted by the government.

The first line drugs mainly drove the cost of ARVs. The cost of second line had a marginal impact on the total cost of care due to the small number of patients which are getting second line treatment: however this number is likely to increase over time with update of viral load.

The cost for other services including nutritional support, training, supervision and logistics (especially transportation of samples and drugs that are crucial to allow the decentralization of care) ranged from one fifth to one third of total costs depending on the method. These critical investments support the necessary infrastructure for delivering services and probably need to be kept at the current level if not increased if the decentralization of AIDS care will be pursued.

The comprehensive care model run by the DREAM program is more expensive than the government ones even if it showed to be very cost-effective because of the ICER lower than the WHO AFR E region GDP threshold. All the components of the comprehensive model considered in the study are able to influence the effectiveness of the program, including the early start of ART due to the efficacy of pre-ART monitoring of CD4 count which is able to prevent the progression to the more advanced stages of HIV/AIDS.

### TABLE 5. Cost-Effectiveness Analysis

| Health Sector Perspective | ICER | Cost per Death Averted |
|----------------------------|-----|------------------------|
| National perspective       |     |                        |
| High estimated             | $1640 | $2556                  |
| Low estimate               | $896  | $1268                  |
| Cost per death averted     | $1395 | $1976                  |

ICER = incremental cost-effectiveness ratio.

### TABLE 6. Sensitivity Analysis

| Variable                           | Baseline | Range, % | ICER | Cost per Death Averted | ICER | Cost per Death Averted |
|-----------------------------------|----------|----------|------|------------------------|------|------------------------|
|                                   |          |          |      | High est | Low est | High est | Low est |
| Baseline                          |          |          |      |           |         |           |         |
| Interest rate                     | 3%       | 0        | $1640 | $2556     | $896    | $1268     | $1395    | $1976    |
| Difference cost per person MW–DREAM | $126    | -30      | $1148 | $1789     | $404    | $776      | $629     | $1209     |
| PPP conversion rate               | 1.96     | -15      | 0     | $126      | $2132   | $3322     | $1388    | $1760     | $2162    | $2742     |
| DREAM patients survival rate      | -5       | -15      | $126  | $2132   | $1486   | $2315     | $741     | $1131     | $1155    | $1735     |
| Difference in survival and retention rate concerning transferred patients in national facilities | +5 | 0 | $126 | $2132 | $1536 | $2357 | $850 | $1193 | $1304 | $1831 |
|                                   | -15      | -15      | $1848 | $2880    | $1103   | $1476     | $1719    | $2299     |

DREAM = Disease Relief through Excellent and Advanced Means, ICER = incremental cost-effectiveness ratio, PPP = purchasing power parity.
advanced clinical stage of the disease in many patients. However, the last WHO guidelines as well as the Malawi NSP are moving towards the “test and treat” approach that makes less useful the use of CD4 count while emphasizes the Viral Load monitoring after starting ART. The Malawi National AIDS control program already planned to achieve about 800,000 patients on treatment by 2020. This objective will be supported by a forecasted budget increase of 43% by 2020, that includes the doubling of funds for laboratory activities that will play a crucial role in the treatment monitoring in order to minimize the rate of non-adherent patients, and will indicate the patients to be shifted to second line because of possible resistances to ARV drugs.

Similarly, the investment in peer-to-peer education and structured retention program could support the scaling-up of the program, that is supposed to put on ART about 300,000 new patients by 2020 to be added on top of the 500,000 currently on ART (see NSP). Such a huge increase of patients number and of the related health personnel workload could easily results in an increase LTFU and non-adherence rates as well as in the staff demotivation. A recent systematic review about retention in care in HIV treatment program stresses the strategic role played by support program in order to minimize treatment abandonment. Social support, home visits and community health workers are all factors associated to higher retention/adherence rate.

Based on the result of this paper the increase for personnel needed for health promotion and peer-to-peer education in the framework of activities focused on improving patients’ retention and adherence should be addressed. This study has several limitations: data on survival of Malawi National program patients on which the calculation of ICER is based, were taken from the literature rather than a prospective comparison with the DREAM program patients. Moreover the mix of new and established patients is different among the two programs and new patients have higher costs. This difference could lead to an underestimation of costs for the DREAM program. The assumption of care costs being constant during the 5 years covered by the study could lead to underestimate the cost dynamic due to economic development of the country as well as the impact of increasing second line treatment use with improved laboratory monitoring. Across cohorts hospitalization costs were omitted. However, overall these factors marginally influence results.

CONCLUSION

The evidence from the DREAM program shows that investing in personnel, implementation of IT routine use, extensive lab monitoring, nutritional supplementation and peer-to-peer education through expert clients is more expensive but can be cost-effective. In the management of chronic diseases there is no the gold bullet, but a combination of innovative approaches can empower the patient, making him or her responsible for care to increase retention and outcomes. HIV comprehensive care can be justified and scaled up. There is also a cost of not investing in quality of care as sub-optimal approaches to HIV care could have a dramatic impact on medium-long term patients’ survival.

The enormous commitment taken by the Global Fund to Fight AIDS, TB and Malaria and others has been critical to ART scale-up. The approach has been mainly quantitative (putting on ART a large number of people). Looking at this study results a qualitative approach should be integrated with a qualitative approach (e.g., considering 5 years survival rate) in order to have consistent evidences on the efficacy of programs. Improving quality of care especially through the use expert clients and structured activities addressed to improve patients’ adherence/retention rate, can represent the next challenge of HIV care program in sub-Saharan Africa.

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