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Abstract

The cost-effectiveness of intervening with a set of HIV/AIDS interventions in low HIV prevalence areas (LPA) and high HIV prevalence areas (HPA) in South Africa is analysed. The rationale for this analysis is to assess the suspected effect of interaction between the intervention and area of implementation, on cost-effectiveness. The paper used the Markov model, which tracked a cohort of patients over their lifetime in each area. Data on costs and health outcomes were collected from the literature, but the distribution of patients in health states at baseline and over time, were based on the patterns observed in the Actuarial Society of South Africa AIDS model (ASSA2008) projections, to depict these interaction dynamics. The effects of recent changes in guidelines of some interventions under consideration were assessed separately outside of modelling and sensitivity analysis conducted on all model parameters. In terms of efficiency, the study found it more cost-effective to intervene in LPA. However, to align efficiency with equity and ethical principles underlying HIV response, more than proportional resources should go into non-ARV based interventions in LPA, while more than proportional resources should go into non-ARV interventions in HPA.

Key words: cost-effectiveness, LPA, HPA health outcomes, simulation, HIV/AIDS, interventions, Markov, prevalence, low, high, South Africa.

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1 Introduction

Tailoring the HIV response to the contexts of the epidemic has been claimed to be one of the best responses to HIV/AIDS (Grassly *et al.*, 2001; Parker & Aggleton, 2002; Walker, 2003). To further efficiency however, such a response is difficult, because of the concurrent influence of the characteristics of the contexts and interventions on costs and health outcomes. In the case of LPA and HPA, these complex relationships imply that the cost-effectiveness of interventions across the two areas is not obvious. In this regard, this paper simulated the costs, health outcomes and cost-effectiveness of a set of HIV/AIDS interventions in these areas in South Africa. These interventions were voluntary counselling and testing (VCT), treatment of sexually transmitted infections (STD), prevention of mother to child transmission (PMTCT), and highly active antiretroviral therapy (HAART).

Globally, HIV/AIDS has resulted in the deaths of about 40 million people since it became prevalent in the early 1980s (UNAIDS, 2010). Some 1.8 million people died from HIV/AIDS in 2009 and in the same year about 2.6 million people contracted new infections worldwide. A recent global report, however suggest that HIV/AIDS growth is stabilising (UNAIDS, 2010:16) as a result of the use of antiretroviral drugs. In 2010, in South Africa, more than 5 million people were living with HIV/AIDS; about 188,000 people died of AIDS in that year whilst about 116,000 new infections occurred (Actuarial Society of South Africa, 2011). Though the impact of HIV/AIDS is still significant, these statistics suggest improvement in HIV outcomes since 2007, in which year 255,000 people died of HIV/AIDS (Actuarial Society of South Africa, 2011). The decrease in mortality is probably a result of recent major undertakings on the part of the South African government, to enhance prevention and treatment.

One of the most notable features of HIV/AIDS has been its differentiated impact across regions, gender, age groups, and income groups, in terms of new infections, prevalence and deaths. During 2009, 95 % of new infections occurred in developing countries. During the same period, sub-Saharan Africa accounted for 67% of all new infections and 75% of all HIV/AIDS-related deaths (UNAIDS, 2010) with the highest prevalence rates (18% to 26%) being found in countries in southern Africa (Alistar & Brandeau, 2010:1). In South Africa, the epidemic impacts to a greater extent on females, younger individuals and some provinces (Actuarial Society of South Africa, 2011).

South Africa has made considerable progress in responding to HIV/AIDS, with more undertakings in 2007, and new guidelines in 2010 and 2011. The usual scarcity of resources implies that these undertakings necessitate new methods of intervention to achieve more outcomes with the limited resources. In this regard, this study proposes allocating resources according to how contexts are efficient with HIV/AIDS interventions. For some time now, there have been proposals to consider contexts of intervention in terms of responding to HIV/AIDS (Grassly *et al.*, 2001:1121). The rationale for these proposals was that an HIV intervention can have different success rates, depending on where it is implemented. In fact, the extent to which an intervention succeeds depends on its

net effect, between the risk factors and its own effect on reducing the impact. Risk factors are diverse, and range from structural factors (Parker *et al.*, 2000; Pronyk *et al.*, 2006; Pronyk *et al.*, 2008; Raogupta *et al.*, 2008), epidemiological, environmental and cultural factors (Airhihenbuwa, 2004; Raogupta *et al.*, 2008). Risk factors have been found to influence health theoretically and empirically through their influence on health-seeking behaviours, including attitudes toward health interventions (Bandura, 1986; Becker, 1974; Geoffard and Phillips, 1996). Risk factors have been thought to be at the centre of differences in new infections, sicknesses and deaths, even in the presence of HIV/AIDS interventions (Airhihenbuwa, 2004).

Calls to respond in context appear more relevant for South Africa. Indeed, South Africa is characterised by a diverse society, diversity in income levels, and, in the context of this paper, diversity in HIV/AIDS prevalence levels. Though a generalised HIV epidemic in South African implies a response targeting the general population (Whiteside & Smith, 2009), prevalence levels in the general population have been consistently different across the provinces. Despite the heterogeneous nature of HIV spreading in South Africa, major HIV interventions undertaken have failed to account for how these interventions would fare in areas with different characteristics. In the context of limited resources to meet HIV/AIDS services' demand, the question revolves around whether HIV/AIDS interventions could be more optimal in some areas of specific prevalence levels, than in others, -a question to be answered by hard evidence on cost and health outcomes in these areas.

2 Methods

Ideally, comparing the cost-effectiveness of intervening in LPA and HPA with a set of interventions entails the following up of cohort of patients for a specific period of time. It then involves, recording costs and health outcomes, in different health states of the progression of HIV/AIDS in each type of area, and, adding up costs and health outcomes. Such a follow-up could be costly and would serve a limited purpose by only reporting costs at specific time of follow-up. In fact, for long- term disease such as HIV/AIDS, policy makers need to plan for the future, and so they need information about costs and health benefits of programmes, beyond what is currently observed. To serve this purpose, it is common to use a model depicting patients' distribution in different health states (for example moderately sick, seriously sick and death) over time, making it possible to integrate evidence on costs and health outcomes (quality of life in a health state for example) from a diversity of sources and then to extrapolate the evidence into the future. To this end, the paper used the Markov State Transition Model.

2.1 Markov model

The model represents patients in health states based on health state levels of influence on costs and health outcomes, and in short and successive periods of the interventions' time horizon. The model determines the costs/health outcomes of a health state, by applying health state costs/ health outcomes to the number of patients in that health state. The number of patients in each health state is obtained by means of the proportion of patients, -called transition probabilities-, who usually fall in that health state from other states, when a cohort of patients is followed up. The costs and health outcomes of any one period of the successive periods are obtained by summing costs/health outcomes of health states in that period. The costs/health outcomes of the model, over the term of analysis, are obtained by summing cost/health outcomes of successive periods.

In tracking over time a cohort of patients in prevention interventions, the Markov model assumed that patients in specific health states transitioned to other states every 3 months. Some patients remained uninfected (NON-INFECTED health state), some became infected but still without AIDS (INFECTEDCD4200+ health state), others had AIDS (INFECTEDCD4200- health state), while others died (DEAD health state). While the main purpose of prevention interventions is to avoid new infections, avoiding costly and worse health outcomes in subsequent use of treatment interventions, has also been acknowledged as benefits of prevention. To show these benefits, treatment-relevant health states were added to the Markov structure of prevention interventions. A typical Markov cycle tree structure for prevention intervention is illustrated appendix 1.

For the HAART intervention, the Markov model assumed a cohort of patients in need of treatment (INFECTED CD4 200-) in which some members, - in a 3 months period-, remained in the same health state, others moved to better health states (INFECTED CD4200+), while others died (DEAD health state). Strata of CD4 counts were used to depict important stages of HIV progression, in line with evidence that the CD4 count is a major predictor of HIV progression (Egger *et al.*, 2002; Hogg *et al.*, 2001). A typical Markov cycle tree structure for treatment interventions is illustrated in appendix 2.

A pair of Markov models was evaluated for each intervention, one model for the HPA and another for the LPA. According to UNAIDS, countries are HPA if the prevalence rate is 3 % and above and LPA if it is below 1% (UNAIDS, 2010; UNAIDS/WHO 2009:20). South Africa is already an HPA according to UNAIDS definitions. Over time, however, prevalence in some provinces has been consistently higher than in others. For this analysis, provinces which had a prevalence rate in the general population of less than 7% in 2007 were classified as LPA, and provinces with prevalence above 7% as HPA. On these grounds, HPA comprised the Eastern Cape, Free State and KZN, then Mpumalanga, Gauteng, and North West while the other provinces comprised the LPA.

The model simulated lifetime (until 95% of the cohort is dead) costs, health outcomes, and cost-effectiveness of intervening in LPA and HPA with a set of the above-mentioned interventions. The simulation tracked these costs and health outcomes in successive three-month periods for a cohort of 10,000 patients

in each area, from 2007. The starting time for the analysis was motivated by the fact that at this time HIV started receiving proper attention by the South African government. The simulation is expected to estimate the economic implications of such a commitment.

2.2 Data and analysis

The transition probabilities (proportions) of patients in HIV health states from other health states were gathered from the literature, especially HIV cohort studies. Transition rates reported for periods other than 3 months, were adjusted to take account of a 3-month period used in Markov model. The rates, i.e. the number of patients who move to a given HIV health state in a period of time, were converted into a 3 months transition probability using the formula $p = 1 - e^{-rt}$ -where p is the transition probability, and r is the rate or the number of patients who transit in a period of time t. The time was transformed in the number of 3 month periods, either through multiplication or division, depending on whether t is greater or less than a 3 months period. The transition probability and their respective sources are in appendix 3.

The costs in health states were also collected from the literature. The paper considered only costs that reflected full opportunity costs of each intervention. Since the South Africa government funds two third of the HIV/AIDS response (Stewart, 2010), the base-case value analysis was considered for the government perspective. However, a societal perspective was also analysed, as per cost-effectiveness expert recommendations (Gold, Siegel, Russel, & Weinstein 1996:166). A societal perspective takes account of full opportunity costs i.e. interventions' and patients' costs. Societal perspective included transport, funeral and waiting time costs in addition to government-perspective costs. Real costs were used in the analysis using 2007 prices and were discounted at 3% in line with the recommendation from cost-effectiveness analysis experts (Gold *et al.*, 1996). Undiscounted results were also reported for the sake of comparison with studies that have reported such results. All analyses were performed using TreeAgePro (DATA TM) software.

The effectiveness in health states was calculated based on the duration in a health state, and the quality of life in this health state. To this end, the quality of life data was extracted from South African literature (Jelsma *et al.*, 2005; Louwague *et al.*, 2007; O'Keefe & Wood, 1996). This data has been collected using instruments that contain descriptive questions, whose answer provides the measure of overall health. The community average health related quality of life (HRQoL) was taken as the average HRQoL from the representative sample.

In cost-effectiveness analysis, however, individual responses need to reflect preferences. Individual responses can be transformed into preference measures or utility indices, using an algorithm that predicts a utility score for a set of responses from an individual. The prediction model was developed based on the responses in a sample of the UK population (Dolan, 1997; Dolan *et al.*, 1995). The same algorithm has been used to produce the value of the responses from the instrument used in South Africa. Using a Europol, an instrument that

asks questions in a health state about mobility, pain/discomfort, in Cape Town, Jelsma *et al.* (2005) produced values of quality of life for patients receiving HAART over a one year period. Using the same instrument in the Free State, Louwague *et al.* (2007) analysed value of quality of life for HIV/AIDS patients, both receiving and not receiving treatment. The paper used these values in different health states of the model. The base case values used in the analysis are in Table1

2.3 Assumptions

Patients' costs/ health outcomes over time depend on patients' distribution in health states under a specific intervention, in a given area. To get this data, the information from the literature was combined with information from the ASSA2008 model projections, to formulate assumptions regarding parameter differential across HPA and LPA. The ASSA suite of AIDS models has been extensively applied in South African HIV/AIDS research (Bradshaw *et al.*, 2004; Groenewald *et al.*, 2005). ASSA2008 is an updated version of a series of AIDS Models of the Actuarial Society of South Africa (ASSA) which improved on ASSA2003. The construction of ASSA2003 was founded on the assumption that the HIV epidemic spreads *via* heterosexual encounters. The modelling distinguished four risk groups (PRO, STD, RSK, and NOT) ranked in descending order of their risk. The PRO, STD, RSK, and NOT groups were: sex workers, frequent carriers of STDs, people at risk but not usually carriers of STDs, and people not at risk, respectively. The model also took account of the differences in the spread of HIV across age, and the gender composition of these risk groups. The model used data on sexual behaviour, on the probability of infection, data on the progression of HIV, on the effect of major interventions, census data (1970, 1996, and 2001), fertility rates, the 1998 and 2001 demographic and health surveys, international migration data, non-AIDS mortality data, and 2008 antenatal survey data in South Africa to formulate such projections. Further to this, the ASSA2008 improved the projections of its predecessors, in that it took account of increased condom usage, treatment with HAART, increases in survival rates among untreated HIV/AIDS patients, and a lower incidence of mother to child transmission than had previously been modelled

Assumptions about the progression of patients in health states were intervention-specific and were based on ASSA2008 projections' growth rate over time in infections, AIDS cases and HIV/AIDS-related deaths. Since the activities of interventions were the same, the costs in the same health states were assumed the same across HPA and LPA, and so was quality of life. The simulation included, however, an assumption of economies of scales in health states, and unit costs moving in an inverse relationship with the number of patients in health states. Because of unavailability of evidence regarding the effect of 2010 and 2011 PMTCT and HAART changes in guidelines, the analysis was conducted under the assumption of 2007 guidelines. The possible effects of these changes were discussed outside of modelling. Uncertainty, expected to arise from any parameter, was handled by probabilistic sensitivity analysis, in which lognormal

distributions and triangular distributions were used for cost and effectiveness values, respectively

3 The results

3.1 The effectiveness

3.1.1 Survival

In an attempt to have the cost-effectiveness of intervening in HPA and LPA well understood, it is worth discussing separately results about the effectiveness and cost of intervening in these areas. Defining effectiveness in terms of survival, the analysis was conducted by comparing survival differences across the areas. The results of such comparisons are presented in Figure 1 below.

As can be seen in Figure 1, the patterns of survival across LPA and HPA are quite different, with greatest differences in patterns of survival apparent in health states NON-INFECTED and health states DEAD. The least differences are observed in health states (INFECTED CD4 200-). Moreover, the pattern of survival appears to be different across interventions. The results show that in general, survival is greater in LPA as compared to HPA.

While it might be speculative to point out the exact reasons for the differences, the results show that the same intervention results in different survival outcomes across LPA and HPA. The results answer partially the paper's initial question on whether the interaction of the intervention and the areas produce an effect on cost-effectiveness. What appears to be the case is that interaction of the interventions and LPA results in more survival than the interaction of interventions with HPA. The results suggest that policy makers in South Africa should take account of the prevalence level in areas, when implementing HIV/AIDS interventions.

Differences in intervention outcomes can be explained by a number of social theories of health behaviour, according to which differences in health status depend on peoples' perception of risk, which in turn depends on personal characteristics (Becker, 1974) or the characteristics of the society in which individuals live (Bandura, 1986). Besides social theories, empirical research has on the other hand reached different conclusions about how interventions interact with cultural norms (Airhihenbuwa, 2004). Other research has concluded that risk behaviour reduction would be greater for people witnessing real threat from the epidemic, in this case HPA (Geoffard & Phillips, 1996; Sweat *et al.*, 2000:113). While some of these conclusions may be relevant to South Africa, what appears to be the fact is that the effectiveness of an intervention depends on the area of such intervention.

In comparing effectiveness of intervening in HPA and LPA using survival for prevention interventions, we cannot ignore that the latter's main purpose is to prevent new infections. However, we can also not ignore the evidence that beneficiaries of different prevention interventions fare differently in treatment interventions (Sweat *et al.*, 2000). To reflect the two facts, the proportion of

non-infected patients over time was compared with the proportion of patients in treatment-relevant health states across HPA and LPA. Figure 2 below illustrates these results. As can be seen in the Figure, LPA results in greater proportions of patients in NON-INFECTED and INFECTEDCD4200- states than does HPA. Moreover, the Figure depicts a fastly decreasing proportion of patients in INFECTEDCD4200- in HPA than it does for LPA. In summary, this suggests that intervening in LPA with prevention interventions not only results in averting greater infections, but also in more future treatment benefits than in HPA. Again, with interventions' activities being the same, this difference in results can be attributed to difference in the interaction between the area type and the intervention.

3.1.2 Survival adjusted with quality of life

The paper also compared effectiveness across areas using survival years adjusted with quality of life. Comparisons using this measure were motivated by the fact that two interventions might achieve the same survival, but a different quality of life. Multiplying survival year in a health state, with the percentage of perfect health in that health state (considered as quality of life), yielded the number of perfect years of life across areas called quality adjusted life years (QALYs). Using QALYs as a proxy for the effectiveness of intervening in LPA and HPA, produced results as presented in Figure 3 below. The results show that QALY output is greater in LPA than in HPA. The greatest differences across areas in total QALYs is observed for non-ARV interventions (STD and VCT), particularly in the health state NON-INFECTED. Once again the fact that QALYs from the same interventions and on the same patients is different across areas, is indicative of different effects on QALYs, and of the interaction between an intervention and the areas of intervention.

3.2 The Costs

While effectiveness analysis is one part of the cost-effectiveness analysis, the analysis is complete when both effectiveness and costs are considered. The cost of intervening in LPA and HPA was analysed. As in the case of effectiveness, the costs of intervening in these areas depended on the distribution of patients, and the unit cost in health states. Assuming an equal unit cost in the same health states across HPA and LPA, implies that the pattern of costs depends on the distribution of patients and the extent of the difference in unit costs across health states. The average costs results of this analysis are summarised in Figure 4 below.

As expected, the average cost is greater in HPA than in LPA. This is because over time, relatively more patients are in costly health states in HPA, than they are in LPA. However, the assumption of the same set up of interventions across the areas, implies similar fixed and variable resources in health states. An implication of this assumption is that different distributions of patients in these health states might result in different unit costs, because of economies of

scales. The paper investigated this question, by assuming an inverse relationship between the growth of patients in health states, and the growth of unit costs in the health states. The Figure 5 below presents the patterns of average cost from the government perspective from which the patterns of a societal perspective can also be understood.

The results suggest different patterns in average costs across LPA with PMTCT and VCT exhibiting the greatest differences. In comparison with previous discussions in this paper, an assumption of economies of scale changes the cost levels, but not the patterns across HPA and LPA except for VCT. It is worth noting an average greater cost for prevention intervention, than would be expected. This is because the paper included subsequent benefits in treatment health states and consequently related costs for prevention interventions, assuming linkages of prevention to treatment.

3.3 Cost-effectiveness

With some understanding of the patterns of cost and effectiveness in the discussion above, the relative cost-effectiveness of intervening in HPA and LPA can now be reviewed. The cost-effectiveness is analysed using, as per literature, the average ratio of cost to effectiveness called the average cost-effectiveness ratio (ACER). The results of Monte Carlo simulation for the government perspective are summarised in Table 2 below.

The results show that prevention interventions result in greater QALYs and smaller costs, than treatment interventions, regardless of the areas in which they are conducted. This is in line with other literature. The results also indicate that intervening in HPA with ARV -based interventions, namely PMTCT and HAART, is less cost-effective. Notable in the results is the different extent of the relative cost-effectiveness ratio across areas. The cost effectiveness ratios of intervening in HPA with PMTCT and HAART are, (calculated based on the values in Table 2), 161% and 197% of the cost-effectiveness ratios of intervening in LPA with the same interventions, based on discounted values. The corresponding percentage for undiscounted values is 162% 400% respectively. By contrast, the cost-effectiveness ratio of STD in HPA is 102% and 97% of the cost-effectiveness ratio in LPA for discounted and undiscounted values. These results have profound implications in policy considerations.

Traditionally, cost-effectiveness analysis has been conducted to help allocate resources. Under budget constraints, the resources allocation principle has been to allocate the next available resources to the most effective intervention, provided it is affordable. While this principle may not fully apply to the context of this research, recent undertakings by the South African government will need more resource inputs, and consequently more efficient management of HIV interventions. A response policy based on efficiency principles that are compatible with the current ethical and equity policy tenets is here proposed. Since intervening in HPA and LPA with non-ARV-based intervention results in less difference in the cost-effective ratio but opposite results occurring with ARV-based interventions, it is more efficient to allocate resources more than

proportionally into ARV-based interventions in LPA on one hand. On the other hand, more effectiveness given the costs will be achieved by allocating resources more than proportionally into non-ARV interventions in HPA.

Given the uncertainty around the parameters used, this paper sought to ascertain the robustness in the conclusion of the study. To this end, the results were recalculated a 1000 times, using each time random values drawn from the distributions of all model parameters on quality of life, transition probability and the costs. The proportions of the number of times intervening in LPA and HPA were more cost-effective are illustrated in Figure 6. This result suggests robustness in the conclusion that intervening in LPA is more cost-effective. The Monte Carlo simulation experiment resulted in 90% to 100% of the times intervening in LPA being more cost-effective.

The above analysis was conducted using PMTCT and HAART implementation guidelines in place until 2010. For the PMTCT, the guidelines consisted of using the single dose Nevirapine around the time of birth, combined with options to or not to breastfeed. In 2010, a more expensive but more effective change to the 2007 guidelines was adopted. It consisted of using a more expensive compound Zidovudine (AZT) from week 14 of gestation, for infected mothers. Some evidence indicates the change in guidelines is effective with persisting infections of 1-2%. However, the way in which they affect cost-effectiveness depends on the relative increase in cost and effectiveness. While their effect on the cost-effectiveness ratio in LPA and HPA is incontestable, the pattern of cost-effectiveness across HPA and LPA does not change, given the unchanged dynamics about the interaction between intervention and areas. The same argument goes for the more expensive but more effective change to HAART guidelines adopted in 2011. These guidelines suggest starting to provide ARVs to patients whose CD4 counts falls below 350

4 Concluding remarks

Given the effect of interaction between an HIV/AIDS intervention and areas of implementation on cost-effectiveness and the lack of cost-effectiveness evidence of intervening in HPA relative to LPA, this study conducted a simulation to compare cost-effectiveness of intervening in these areas, using a set of HIV/AIDS interventions in South Africa. The simulation was based on the dynamics between the intervention and the areas' characteristics, and on a combination of information from the literature and an AIDS projection model of the Actuarial Society of South Africa (2011). The simulation results revealed that intervening in LPA was more cost-effective. The evidence in the literature that interventions do better where there are more patients to take advantage of economies of scale was not supported in this study.

To align efficiency with equity and ethical principles underlying HIV response, policy implication was that more than proportional resources should go into non-ARV based interventions in LPA whilst more than proportional resources should go into non-ARV interventions in HPA. These results were

checked for robustness by means of Monte Carlo simulation which showed that these results could be reliable with a probability of between 90 and 100%. Moreover, the analysis was based on the interventions' guidelines in place in 2007 which did not include recent changes notably on PMTCT and on early provision of antiretroviral. An analysis of possible implication of these change suggested that the conclusion of the study would not change.

As a policy implication, South African government should abandon the policy of intervening in areas ignoring the potential effect of the interaction between a specific intervention and the areas of intervention on the costs and effectiveness outcomes.

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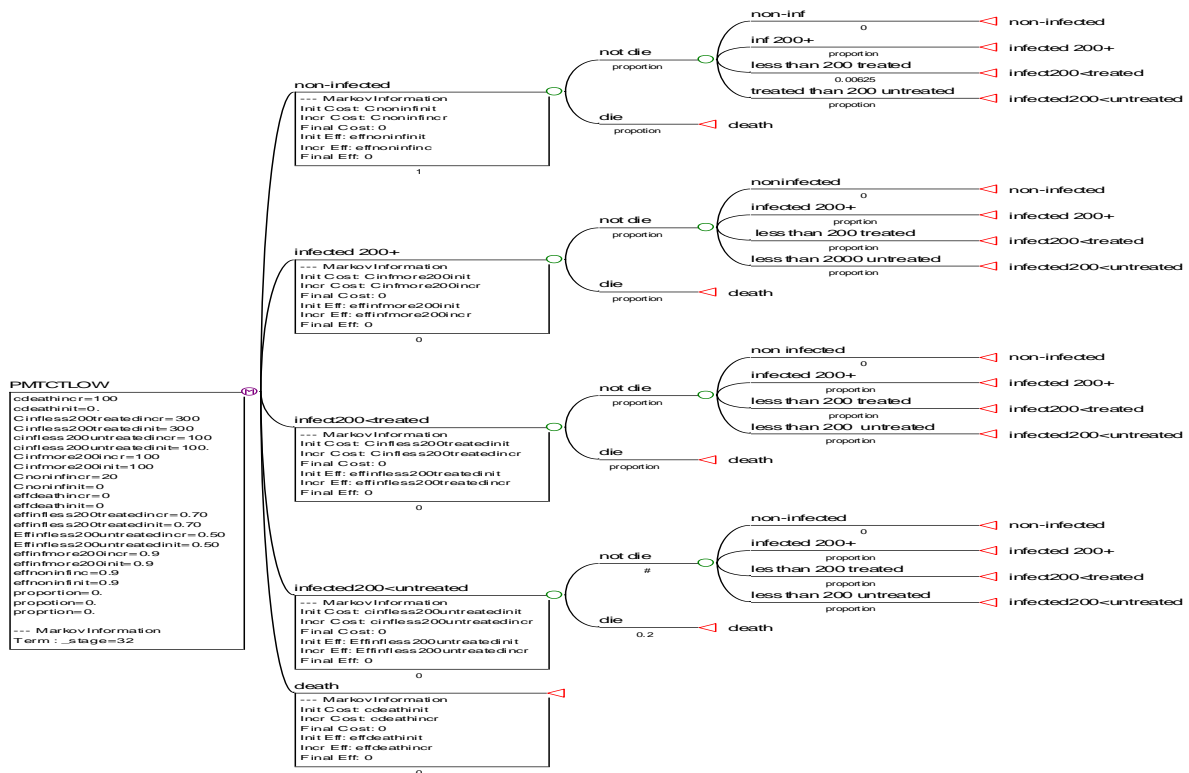
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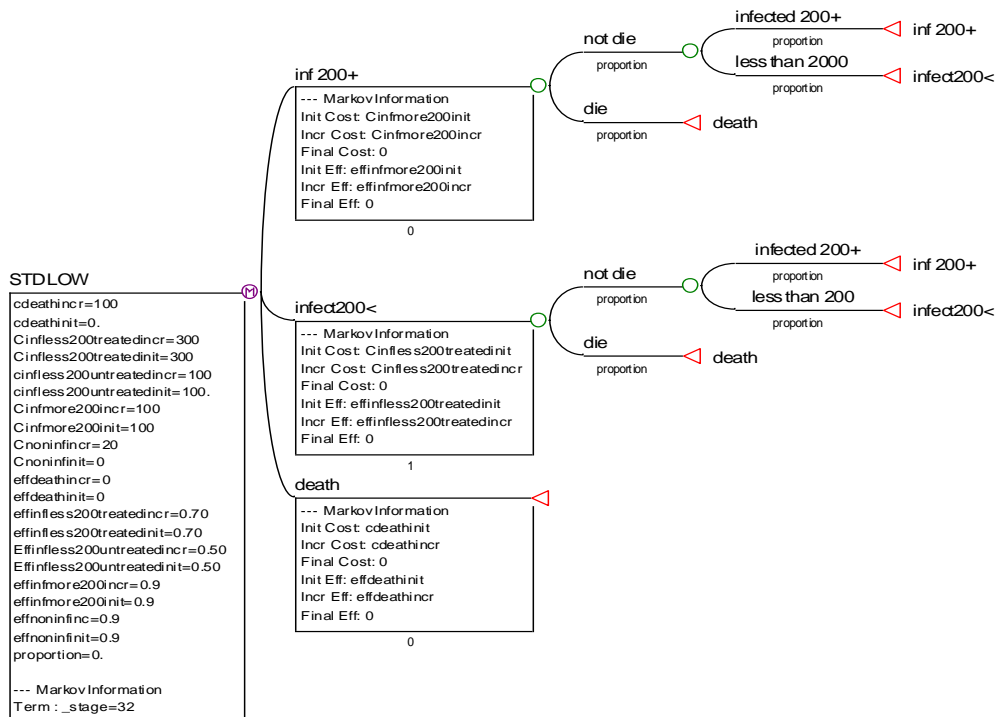
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Appendix 1: Markov Model Structure of a typical Prevention Intervention.



Appendix 2: Markov Model Structure of a typical HAART intervention.



Appendix 3: Baseline sources of transition probabilities ¹

Non-infected to infected. (NON-INFECTED- INFECTEDCD4200+)

VCT (sources: Actuarial Society of South Africa (ASSA), 2011, Rehle et al, 2007): The transition probabilities were based on the annual infection rate in the general population in South Africa.

STD (Sources: Johnson, 2008, Gilson et al, 1997): The transition probabilities were based on the rate at which patients who are under STD treatment acquire HIV/AIDS infections.

PMTCT (Sources: Human Science Research Council (HSRC), 2005, Actuarial Society of South Africa, 2011, Meldrum 2004, Health System Trust (HST), 2011). The transition probabilities were based on the transition from infected to no-infected for new born and the effectiveness of mother to child transmission interventions in the country.

Infected to need of treatment (INFECTED 200+, INFECTED CD4200-):

Source: Adam and Johnson 2009. Transition probabilities were based on Markov model to determine the proportion of patients needing treatment by representing the infected into compartments based on current CD4 counts clinical status.

Need of treatment to treated (INFECTED CD4 200- TO INFECTED CD4200- TREATED)

Need of treatment to untreated (INFECTED CD4 200- TO INFECTED CD4200- UNTREATED)

Sources (Actuarial Society of South Africa, 2011, UNAIDS 2011): The transition probabilities were based on the proportion of patients in need of treatment who get treatment and the proportion of patients in need of treatment who do not get treatment.

Infected on treatment to death (INFECTED CD4200- TO DEATH).

Sources: Cleary et al 2004, 2006. Transition were estimated over a three-month period from Kaplan Meier product Limit estimates of survival for 1729 patients accessing ART in the first 48 months in Kyayelitsha.

Intermediate transition probabilities.

Sources: imputation. Given that all transition probabilities from one health state to other health states sum to 1 in Markov state transition model, some of the missing probabilities were obtained through imputation.

¹ The transition probabilities were adjusted for the HPA and LPA based on the differential in modelled HIV/AIDS impact in these areas by ASSA2008 AIDS model.

Table 1: Quality of life (1), Transition Probabilities (2) Government Perspective costs (3) and societal Perspective costs (4) for the first 3-month period.

HAART high prevalence					HAART low prevalence			
	Inf >200+	Inf <200	Death		Inf >200+	Inf <200	Death	
Inf >200+	(1) 0.90 (2)0.925 (3)100 (4)150	(1) 0.70 (2)0.0615 (3)365 (4)465	(1) 0.0 (2)0.0197 (3)0 (4)704		Inf >200+	(1) 0.90 (2)0.960 (3)100 (4)150	(1) 0.70 (2)0.0482 (3)365 (4)465	(1) 0.0 (2)0.000612 (3)100 (4)704
Inf <200	(2) 0.00001	(2) 0.960	(2) 0.055		Inf <200	(2)0.00001	(2)0.920	(2) 0.039
Death	(2) 0.0	(2) 0.0	(2) 1		Death	(2)0	(2)0	(2) 1

STD high prevalence						STD low prevalence				
	Non infect	Inf >200+	Inf <200	Death		Non infect	Inf >200+	Inf <200	Death	
Non infect	(1) 0.90 (2)0.985 (3)17.5 (4)28.5	(1) 0.90 (2)0.0145 (3)17.5 (4)28.5	(1) 0.70 (2)0.0001 (3)365 (4)465	(1) 0 (2).00042 (3)100 (4)704		Non infect	(1) 0.90 (2).992 (3)17.5 (4)28.5	(1) 0.90 (2).0077 (3)17.5 (4)28.5	(1) 0.90 (2).0001 (3)385 (4)465	(2) 0.00022 (3) 100 (4) 704
Infect 200+	(2) 0	(2) 0.91	(2)0.011	(2)0.009		Infect 200+	(2) 0	(2) 0.95	(2) 0.009	(2) 0.003
Infect 200-	(2) 0.0	(2) 0.00001	(2) 0.92	(2) 0.09		Infect 200-	(2) 0	(2) 0.0001	(2) 0.90	(2) 0.028
Death	(2) 0	(2) 0	(2) 0	(2) 1		Death	(2) 0	(2) 0	(2) 0	(2) 1

VCT high prevalence						VCT low prevalence				
	Non infected	Infected >200+	Infected <200	Death		Non infected	Infected >200+	Infected <200	Death	
Non infected	(1) 1 (2)0.95 (3)30 (4)40	(1) 0.90 (2)0.00416 (3)30 (4)40	(1) 0.70 (2)0.00006 (3)365 (4)465	(1) 0 (2)0.00002 (3)0 (4)704		Non infected	(1) 1 (2)0.98 (3)30 (4)40	(1) 0.90 (2) 0.00639 (3)30 (4)40	(1) 0.70 (2) 0.00001 (3)365 (4)465	(1) 0 (2) 0.00001 (3) 100 (4) 704
Infect ed 200+	(2) 0	(2) 0.98	(2)0.001	(2)0.0009		Infect 200+	(2) 0	(2) 0.99	(2) .0003	(2) .0005
Infect 200-	(2) 0	(2) 0.0001	(2) 0.98	(2) 0.09		Infect 200-	(2)0	(2) 0.00001	(2)0.92	(2)0.05
Death	(2) 0	(2) 0	(2) 0	(2) 1		Death	(2) 0	(2) 0	(2) 0	(2) 1

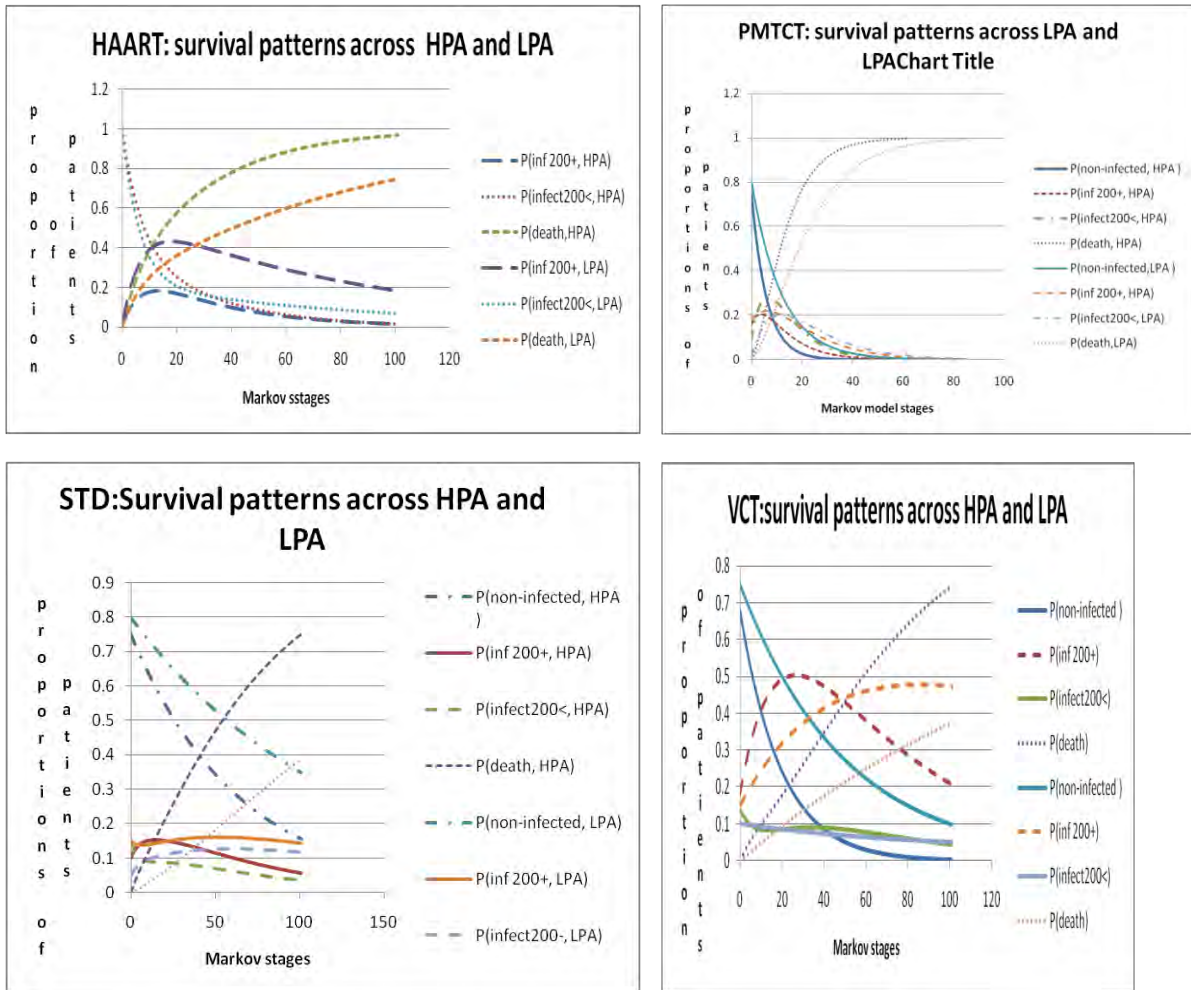
PMTCT high prevalence						PMTCT low prevalence				
	Non infect	Inf >200+	Inf <200	Death		Non infect	Inf >200+	Inf <200	Death	
Non infect	(1) 0.90 (2)0.85 (3)100 (4)120	(1) 0.80 (2)0.08 (3)100 (4)120	(1) 0.60 (2)0.0001 (3)365 (4)465	(1) 0 (2)0.0042 (3)10 (4)704		Non infect	(1) 0.90 (2)0.92 (3)100 (4)120	(1) 0.80 (2)0.06 (3)100 (4)120	(1) 0.60 (2)0.0001 (3)365 (4)465	0.001 100 700
Infect 200+	(2) 0	(2) 0.79	(2)0.009	(2)0.09		Infect 200+	(2) 0	(2) 0.85	(2)0.006	(2)0.06
Infect 200-	(2) 0.0	(2) 0.00001	(2) 0.90	(2) 0.11		Infect 200-	(2) 0.0	(2) 0.00001	(2) 0.91	(2) 0.09
Death	(2) 0	(2) 0	(2) 0	(2) 1		Death	(2) 0	(2) 0	(2) 0	(2) 1

Table 2: Lifetime costs and Effectiveness

Intervention	HPA C (\$)	HPAE (QALYs)	HPA ACER (\$/1 QALY)	LPA C (\$)	LP AE (QALYs)	LPA ACER (\$1/QALY)
VCT						
Discounted 95% CI	522 (98.72-2095)	4 (2-5)	130.50	400 (62.-- 1898)	5 (2-7)	80
Undiscounted 95% CI	1525 (375-5763)	10 (5-13)	152.3	1211.16 483-4490	5 (3-6)	242
STD						
Discounted 95% CI	430 (90-1836)	4 (2-6)	107.50	525 (67- 2533)	5 (2-7)	105.00
Undiscounted 95% CI	1291 (356-5084)	10 (5-14)	129.1	1743 (256- 8445)	13 (6-18)	134.07
PMTCT						
Discounted 95% CI	263 (144-460)	1 (0-1)	263	489 (170- 2250)	3 (2-3)	163
Undiscounted 95% CI	789.44 (432-1379)	2 (1-3)	394.72	1211.16 (483- 4490)	5 (3-6)	242.23
HAART						
Discounted 95% CI	9092.72 (8924-9647)	2 (1-3)	4546.36	1257 (146- 6879)	3 (2-4)	635
Undiscounted 95% CI	24410 (24049- 25030)	5 (3-7)	5424.60	2657 (493- 13125)	2 (4-11)	1328.50

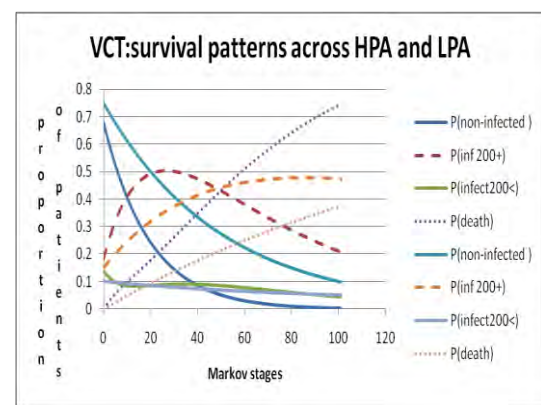
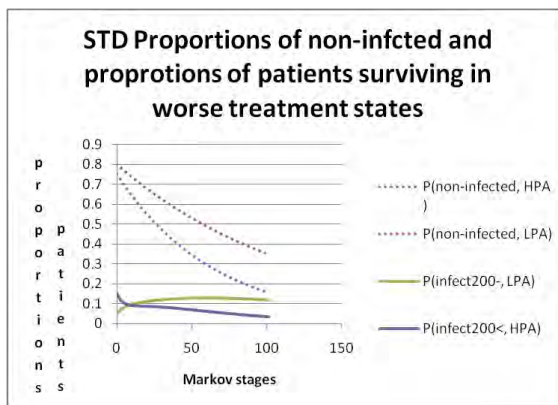
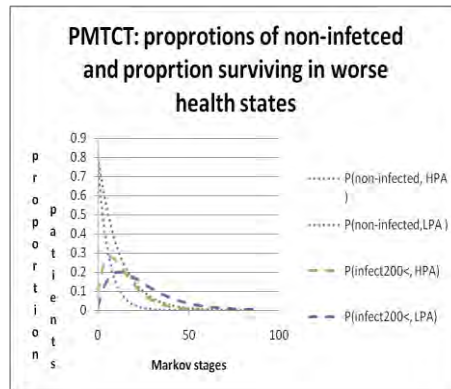
Source: this study analysis based on data collected from the Literature and information from the ASSA2008. LPAC: low Prevalence areas cost, LPE: low Prevalence area Effectiveness, LPAACE: low prevalence area average Cost-Effectiveness, HPAACE: high Prevalence areas average Cost-Effectiveness

Figure 1: Survival patterns in LPA and HPA Prevalence areas of South Africa:



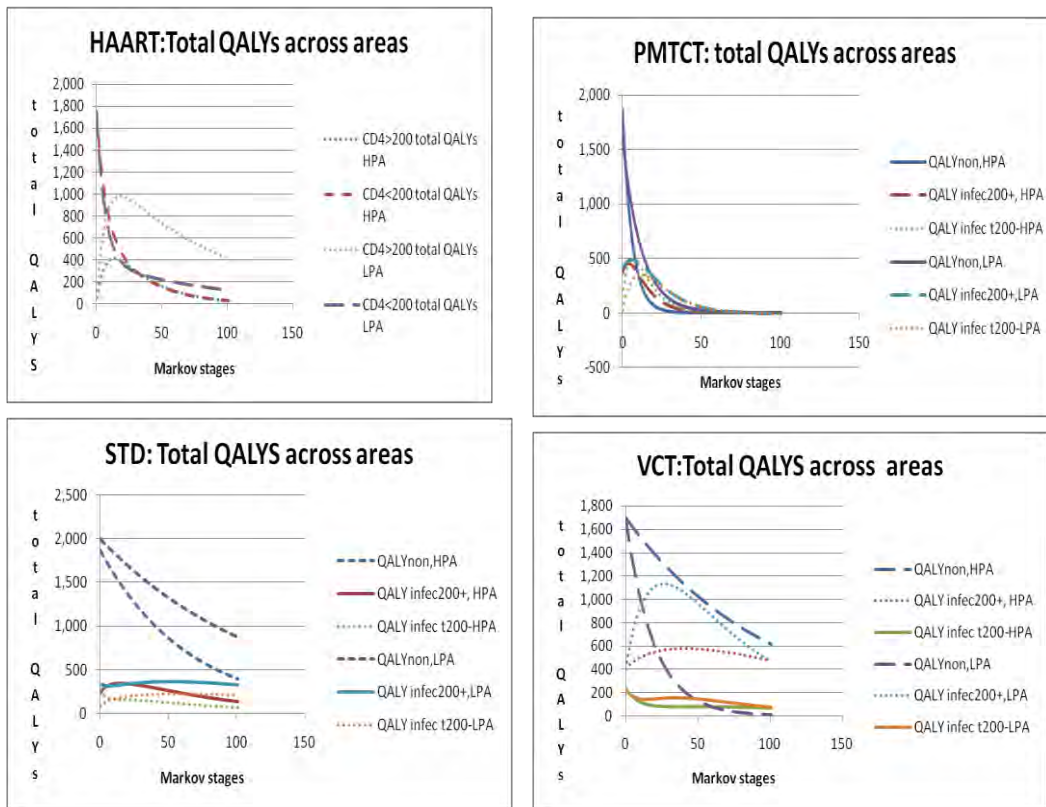
Source: Study Analysis based on Transition Probabilities in health states.

Figure 2: Proportions of Non-Infected Infected (PNI) and Surviving (PS) patients in Treatment-Relevant States



Source: the study Analysis based on Transition Probabilities

Figure 3: Comparisons of quality adjusted life years across LPA and HPA.



Source: the Study Analysis based on Transition Probability and Quality of life data

Figure4: The Average costs in Health States (Government and Societal Perspective) Comparisons across LPA and HPA.

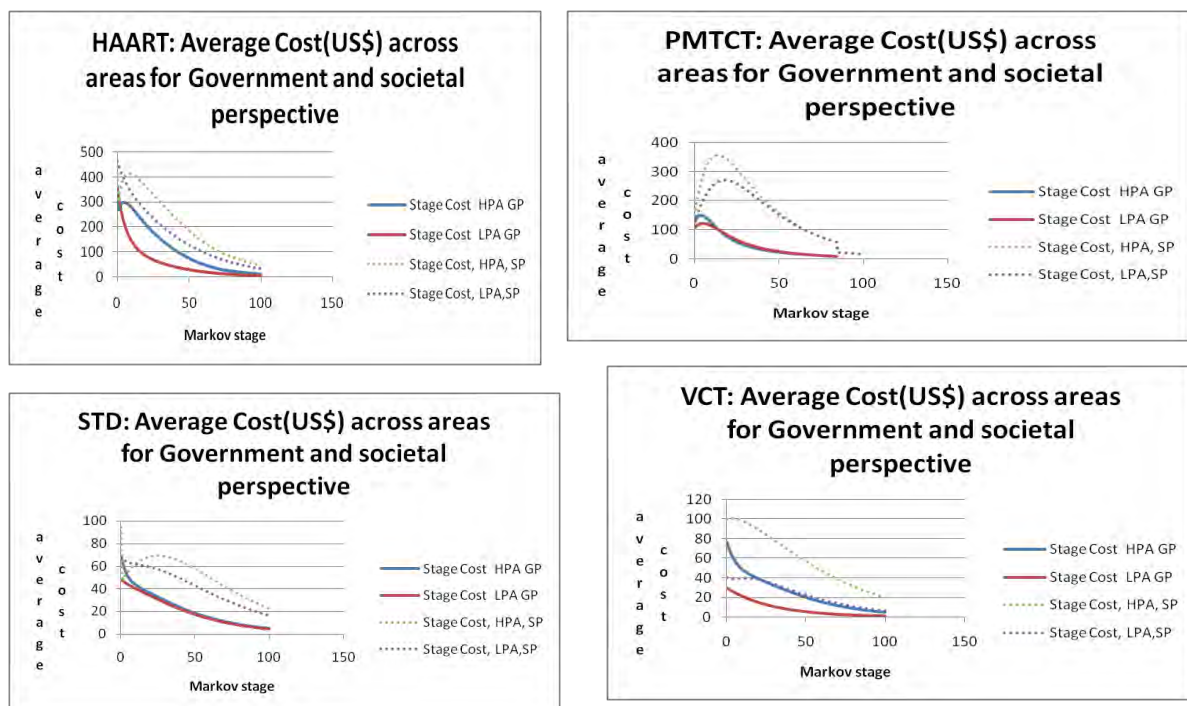


Figure 3.5 The average costs of intervening in HPA and LPA

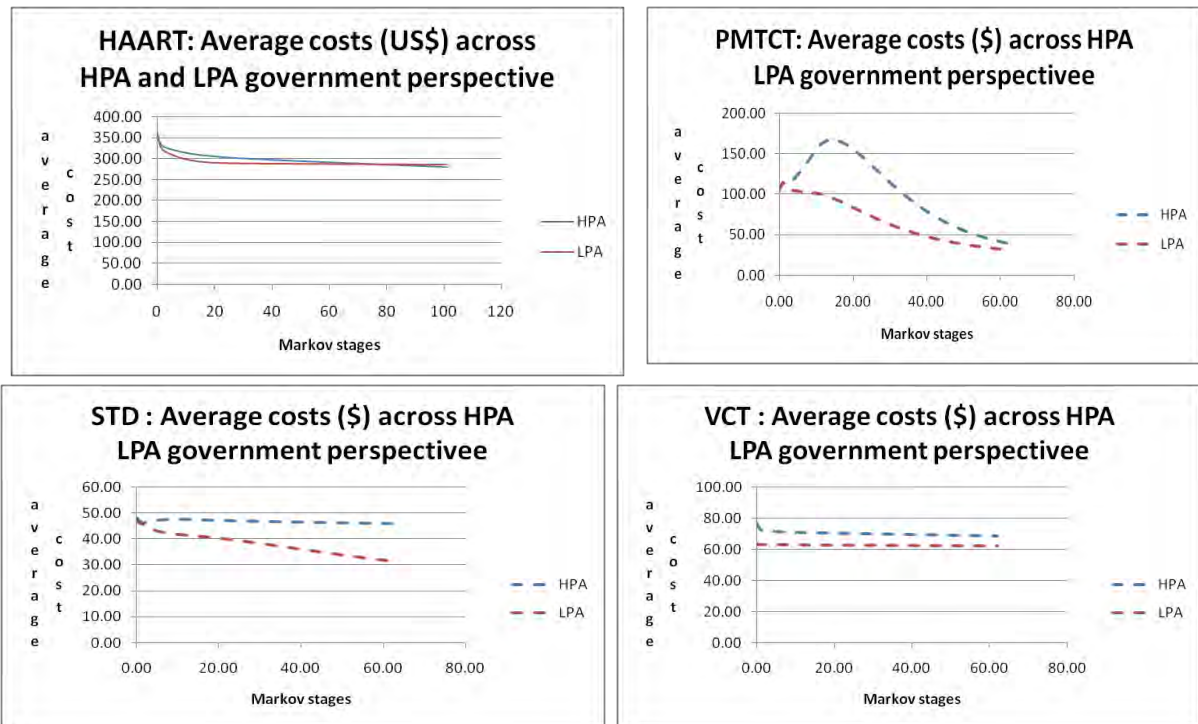
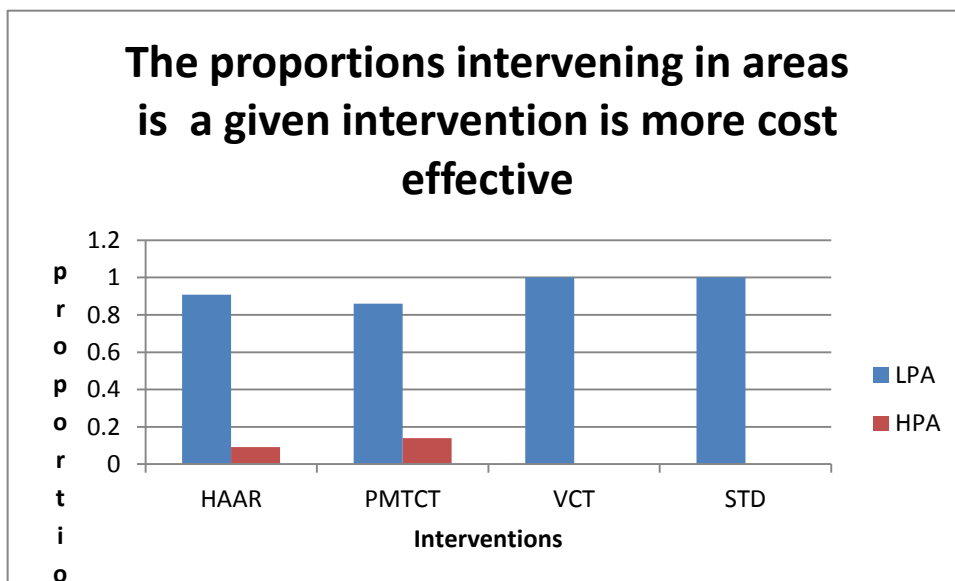


Figure 6: Results of Sensitivity Analysis of the Conclusion of this study



Source: Results of this study obtained through a Monte Carlo simulation of Costs and Effectiveness results. ²

² The analysis focuses only on guidelines because data for more recent ARV guidelines are not available. This is analyzed in the paper based on assumptions.