Relative Costs, Health Outcomes and Cost-Effectiveness of HIV/AIDS Interventions in Rural and Urban Areas in South Africa

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***Abstract*— The literature has long argued that the effectiveness of HIV/AIDS interventions depends on the contexts of their implementation. However, estimates of the relative costs, effectiveness and cost-effectiveness of HIV/AIDS interventions in socio-economic contexts such as rural and urban areas in South Africa are insufficient to guide policy makers in resource allocations. This paper uses Markov states transition models to provide and compare such estimates for prevention of mother-to-child transmission (PMTCT), highly active antiretroviral therapy (HAART) for adults, and HAART for children. Data for the baseline costs and health outcomes are collected in the literature. To capture the effect of a given HIV/AIDS intervention and the area of its implementation, transitions in HIV/AIDS states over time are pegged to projections of Spectrum Policy Modeling System in that area. The results suggest that the extent to which cost-effectiveness of HIV/AIDS interventions across a rural area and an urban area are different is great. Policy makers should allocate resources according to these CE variations.**

***Index Terms*— cost-effectiveness, South Africa, urban, rural,**

INTRODUCTION

THE amount of resources committed to HIV/AIDS by the South African government, as part of its effort to reduce the impact of the epidemic, has been increasing since 2007. Further efforts in resource management are however required in order to maximise health outcomes from available resources. One of such efforts is to intensify resources in rural and urban areas according to the relative cost-effectiveness of HIV/AIDS interventions in such areas. This approach to policy making is however facilitated by relative cost-effectiveness estimates, which have not been produced for major HIV/AIDS interventions. This paper aims to provide such estimates..

The impact of HIV/AIDS in South Africa, though stabilizing, remains high. The prevalence of HIV/AIDS in the general population grew from almost 0 in 1985 to 11.2% in 2007 and stabilized around this level since [1]. With prevalence being the sum of new infections and surviving HIV population, stabilization of prevalence in the era of HAART-induced survival implies a reduction in the infection rate. The number of annual new infections was estimated at 511,000 in 2000, 101,000 in 2013 and is projected decrease to 61,235 in 2020 [2]. The number of annual AIDS deaths were estimated to be 118,000 in 2000, 196, 000 in 2013 and is projected to be 135,000 in 2020 [2]. Significant reduction of the impacts of HIV/AIDS requires more commitment to the response. The usual scarcity of resources coupled with an unfavorable economic outlook both nationally and internationally implies that such commitments focus on approaches to manage available resources efficiently. Intensifying resources in rural and urban areas in South Africa according to how HIV/AIDS interventions are relatively cost-effective in these areas is one of such approaches as informed by theoretical explanations and some empirical evidence. .

Theoretical expositions insinuate that the cost-effectiveness in socio-economic areas, such as a rural area and an urban area, are due to be different. The theory of the socio-economic determinants of health proposes that the impact of HIV/AIDS is lower in an area with higher socio-economic status [3], an urban area for example. The theory predicts that factors prevailing in a higher socioeconomic status such as high levels of income, education, are conducive to favorable health conditions and avoidance of risky behaviour. This prediction implies that the impact of HIV/AIDS is higher in a rural area than it is in an urban area. It further implies that the effectiveness of an HIV/AIDS intervention is lower in a rural area than it is in an urban area, on the understanding that the effectiveness of an HIV/AIDS intervention is measured as the extent to which it reduces the impact of HIV/AIDS. Lower reduction in the impact of HIV/AIDS in a rural area by a standard HIV intervention for a rural area and an urban area is explained by more impact of HIV/AIDS in a rural area and by the unlikelihood of the standard intervention to address specifically factors causing difference in the impact of HIV/AIDS across areas. .

The difference in the impact of HIV/AIDS across a rural area and an urban area as a result of interaction between the intervention and the area implies also the difference in costs across areas. The difference in the cost of an HIV/AIDS intervention in a rural area and an urban area can be grasped through the realization that an HIV/AIDS intervention earmarks specific activities to the impact. For example,

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specific procedures are earmarked to patients whose CD4 count has reached a critical stage while a set of procedures are planned for patients with mild conditions. Since these impacts of HIV/AIDS are caused or originate from contextual factors and since this health impacts influence the activities of an HIV/AIDS intervention, contextual factors influence the costs of HIV/AIDS interventions. The difference in the extent of these factors across areas implies that areas may influence differently the costs of an HIV/AIDS intervention.

The above prediction of the theory of socio-economic determinants of health is founded on the assumption that contextual factors influence on average individual behaviours and attitudes towards HIV/AIDS intervention in a similar manner. This may however not be always the case. Other theories formulate individual-specific factors which act independently of the contextual factors. Psychosocial theories for example explain that risk behaviours or attitudes towards HIV interventions depend on the individual ability and willingness to learn about change in such behaviours or attitudes ([4], [5], [6]). Economic theory explains that unsafe risk behaviour, i.e. risky sexual behaviour or risky attitude towards health interventions, is based on the cost and utility analysis between sexual partners, or the cost and utility analysis of patients with respect to using a specific HIV/AIDS intervention ([7],[8],[9],[10],[11]). Epidemiological theories focus less on individual behaviours but on epidemic behaviour, thus highlighting the fact that the risk of infections and the effectiveness of interventions depend largely on HIV prevalence within particular area [12]. These theoretical exposés imply complex outcomes from interaction of each area factors and an HIV/AIDS intervention, which in turn entail potential variation in cost-effectiveness of HIV/AIDS interventions across areas. Variation in cost-effectiveness of an HIV/AIDS intervention across rural area and an urban area brings about opportunities to increase efficiency in resource allocations.

Empirically, studies showed that the effectiveness of HIV/AIDS interventions depend on the area or context of implementation ([13], [14]). The evidence revealed that most of the factors underlying the impact of HIV/AIDS in a given context prevail in patterns that are different from the patterns in another context and that these factors indirectly influence the impact (effectiveness) of HIV/AIDS interventions [15]. For instance, one study comparing the effectiveness of treating STDs to prevent HIV transmission in a low prevalence area (Tanzania) and a relatively high prevalence one (Uganda) found that the treatment of STDs reduced HIV transmission to a greater degree in Tanzania than in Uganda [16]. The factors underlying the difference in effectiveness was that in the latter country, HIV transmission was taking place outside the core groups with high STI rates, which were being targeted by STI interventions [16]. Even in comparable socio-economic areas, evidence showed that the impact of HIV/AIDS and implied effectiveness of HIV/AIDS interventions were different. Reference [17] found that risk factors such as early sexual debut were important determinants of infections in urban populations with high prevalence (Ndola and Kisumu) while these factors were less important in urban populations with low HIV prevalence (Cotonou and Yaoundé), making prevalence a factor likely to explain difference in effectiveness of HIV/AIDS interventions across these similar socio-economic areas. Cost-effectiveness evidence has also varied across areas with not consistent explanation of the differences ([18], [19], [20]).

Theoretical uncertainty and empirical insights above insinuate potential variation in cost-effectiveness of HIV/AIDS interventions across a rural area and an urban area in South Africa, which would be crucial to policy making. In fact, if cost-effectiveness of HIV/AIDS interventions varies to great extent across rural and urban areas, it would provide policy makers with an opportunity to increase efficiency in resource allocations by intensifying resources according to how cost-effectiveness of HIV/AIDS interventions compares in these areas. This relative cost-effectiveness evidence has however remained insufficient and this paper contributes to its estimation. .

I. Methods

Such estimation requires a follow up of patients in HIV/AIDS interventions in each area over time and a record of costs and health outcomes. As this is costly and can only provide estimates up to the point of follow up while policy makers need estimates that incorporate long term for planning purpose, modeling is an alternative. This paper uses Markov states transition models.

A Markov states transition model tracks a hypothetical cohort of patients in successive periods (cycles) of equal intervals over a specific time horizon of an HIV/AIDS intervention. In each cycle, the hypothetical population is distributed in mutually exclusive HIV/AIDS states, i.e. a patient cannot be in two HIV/AIDS states in one period. In each period, costs and health outcomes relevant to a given HIV state are applied to the number of patients in that state. The costs and health outcomes of successive periods are then summed up. In case many Markov models are used, the results of the models are compared. Markov modeling is appropriate for chronic diseases in which patients move fort and back in different health states ([21], [22]) such as HIV/AIDS. Markov modeling has been extensively used in the literature to model HIV/AIDS interventions ([23], [24], [25], [26], [27], and [28]).

In this paper, hypothetical cohorts of patients are tracked over time in various HIV/AIDS states using Markov states transition models. Specifically, two pairs of Markov states transition models are constructed for each intervention. One pair of models is analysed in a rural area and another pair in an urban area. In each area, one Markov states transition model tracks a hypothetical cohort of 100,000 patients in successive three-month periods over the lifetime of the cohort (until 95% of patients die) in an HIV/AIDS intervention. Another model tracks a hypothetical cohort of 100,000 patients in successive three-month periods over their lifetime in USUAL CARE. The cohort is assumed to be similar to the population of patients who would have been using HIV/AIDS interventions since 2007. The year 2007 is chosen as the starting point of simulation because it is the year which marked the South African Government's serious commitment to tackle the HIV epidemic [29]. This study aims to advise South African policy makers on the economic implications of such a commitment. The interventions modeled are PMTCT, HAART FOR ADULTS and HAART FOR CHILDREN.

For PMTCT, patients are tracked in "uninfected', "infected", "AIDS" and "dead" HIV/AIDS states and those who develop AIDS are directly linked to care. It is assumed that a cohort of 100,000 pregnancies in infected mothers starts in the "uninfected" state; within 3 months, some progress to the "infected" state, others to the "AIDS" state and others to the "dead" state. The cohort of HIV-positive pregnant women is assumed to be on dual therapy PMTCT consisting of Zidovudine (AZT) at 28th week of pregnancy and during labour, followed by Nevirapine (NV) for the new-born baby. The cohort is assumed to reflect HIV-positive pregnant women in South Africa for 2007 in each area. Of these women, 20% exclusively breastfeed, 62% exclusively use formula milk and 18% use mixed feeding [30]. It is assumed that in the absence of PMTCT, patients use USUAL CARE (antenatal care) in which case the Markov states transition model tracks these patients in similar HIV/AIDS states modeled for PMTCT.

For HAART FOR ADULTS, a cohort of 100,000 HIV infected adults starts in the "AIDS" state, that is, when their CD4 count is below 200 . Then, in each of the successive 3-month periods, some members of the cohort remain in the HIV/AIDS state; others improve in health status to CD4 count above 200, that is, to "non-AIDS" while the rest worsen to "dead" HIIV/AIDS state. The cohort is assumed to have the socio-economic characteristics of HIV infected adults in 2007. In the absence of HAART FOR ADULTS, patients use usual health care services in which case the Markov model tracks these patients in similar HIV/AIDS states modeled for HAART FOR ADULTS.

For HAART FOR CHILDREN, a cohort of 100,000 HIV infected children starts in the "AIDS" state. Then, in each of the successive 3-month periods, some members of the cohort remain in the "AIDS" state; others improve in health status to "non-AIDS" state while the rest worsen to "dead" state. AIDS in children is defined as a stage at which there is severe illness, that is, stages 3 and 4 of the WHO (WHO, 2005). It is assumed that the cohort uses pediatric care (USUAL CARE) in the absence of HAART FOR CHILDREN in which case the Markov model tracks these patients in similar HIV/AIDS states modeled for HAART FOR CHILDREN. The cohort is assumed to have the socio-economic characteristics of HIV infected children in 2007.

The base-line costs and health outcomes, i.e. the costs and health outcomes in the first three-month Markov period are estimated on the basis of cost, health outcomes evidence collected in the literature. The hypothetical cohort is applied to the proportion of patients (transition probabilities) in each HIV/AIDS state to determine the number of patients in that HIV/AIDS sate. Then cost data and health outcomes relevant to each HIV/AIDS state from the literature are applied to patients in that HIV/AIDS state to determine the cost, health outcomes of the first three-month Markov period. Table 1-Table 3 provides a summary of transition probabilities, costs and health outcomes (quality of life) for each model. Though costs, transition probabilities and health outcomes are collected from many sources, Table 1-Table 3 show only few sources. The source(s) cited is (are) selected on the basis that it (they) contains the best evidence or has (have) a value close to an average of values from different sources.

Table: 1 Transition probabilities data for the base-case comparison (PMTCT, HAART FOR ADULS and their related USUALCARE)

PMTCT	Rural context			Urban context		
Transition probability	Base – case Values (BCV)	Range	Source	Base-case values (BCV)	Range	Sources
Non-infected to infected	0.036	0.029-0.041	[31]	0.030	(0.029-0.041)	[32]
Non-infected to death	0.18	0.10-0.25	Model derived	0.12	(0.10-0.25)	Model derived
Infected to AIDS	0.07	0.06-0.10	[31]	0.05	(0.04-0.10)	[30]
Infected to death	0.06	0.06-0.10	[31]	0.05	(0.04-0.10	[33]
AIDS to deaths	0.20	0.10-0.30	[31]	0.13	(0.5-0.30	[18]
USUAL CARE	Rural context			Urban context		
Transition probability	BCV	Range	Source	BCV	Range	Source

Non-infected to infected	0.33	(0.25-0.40)	[33]	0.28	(0.25-0.50)	[33]
Non-infected to death	0.18	(0.10-0.20)	[33]	0.12	(0.10-0.15)	[33]
Infected to AIDS	0.07	(0.06-0.10)	[33]	0.05	(0.02-0.09)	[33]
Infected to death	0.06	(0.06-0.10)	[33]	0.05	(0.01-0.08)	[33]
AIDS to deaths	0.20	(0.10-0.30)	[34]	0.13	(0.08-0.18)	[34]
HAART FOR ADULTS	Rural context			Urban context		
Transition probability	BCV	Range	Source	BCV	Range	Source
Non-AIDS to AIDS	0.01	(0.009-0.10)	[35]	0.001	(0.001-0.10)	[27]
Non –AIDS to death	0.01	(0.001-0.10)	[36]	0.001	(0.001-0.10)	[27]
AIDS to non-AIDS	0.10	(0.05-0.30)	Model derived	0.15	(0.05-0.30)	Model imputed
Aids death	0.02	(0.001-0.10)	[37]	0.009	(0.001-0.10)	[27]
USUAL CARE	Rural context			Urban context		
Transition probability	BCV	Range	Source	BCV	Range	Source
Non-AIDS to AIDS	0		Assumption [1]	0		Assumption
Non –AIDS to death	0		Assumption	0		Assumption
AIDS to non-AIDS	0		Assumption	0		Assumption
AIDS to death	0.15	(0.05-0.25)	[27]	0.12	(0.05-0.25)	[27]
HAART FOR CHILDREN	Rural context			Urban context		
	values	Range	source	Value	Range	Sources
Non-AIDS to AIDS	0.01	(0.009-0.10)	[35]	0.001	(0.001-0.10)	[27]
Non –AIDS to death	0.01	(0.001-0.10)	[36]	0.001	(0.001-0.10)	[27]
AIDS to non-AIDS	0.10	(0.05-0.30)	Model derived	0.15	(0.05-0.30)	Model imputed
Aids death	0.02	(0.001-0.10)	[37]	0.009	(0.001-0.10)	[27]
USUAL CARE	Rural context			Urban context		
	Value	Range	Sources	values	range	Sources
Non-AIDS to AIDS	0		Assumption	0		Assumption
Non –AIDS to death	0		Assumption	0		Assumption
AIDS to non-AIDS	0		Assumption	0		Assumption
AIDS to death	0.15	(0.05-0.25)	[27	0.12	(0.05-0.25)	[27]

Table 2 Three-month cost data for the base-case comparison (government perspective)

PMTCT intervention				
	Rural context		Urban context	
HIV/AIDS states	Base-case value	Source	Value	Sources
Non –infected	$200(100-300)	[38]	250 (100-300	[40]
Infected	$200 (100-300)	[34]	250 (100-300)	[40]
AIDS	$350(100-300)	[34]	400 (200-500)	[41]
Death	$50 (0-100)	[39]	75 (0-100)	[39]
USUAL CARE				
HIV/AIDS state	Value	Source	Value	Sources
Non –infected	$200(100-300)	[42]	250 (100-300	[43]
Infected	$200(100-300)	[42]	250 (100-300)	[45]
AIDS	$375(100-300)	[28]	425 (200-500)	[27]
Death	$50 (0-100)	[39]	75 (0-100)	[44]

[1] The literature documents that in the absence of HAART, no patients who start in the AIDS state would move to Non-aids State. Such patients would instead see their health deteriorates [27] (Badri *et al*., 2006: 65). Since no patients move from AIDS to non-AIDS in USUAL CARE, so no patients would transit from non-AIDS to any other HIV state.

Note: The cost in "death" was considered as once-off cost in the estimation of the cost for the cohort.

Table 3 Quality of life data used in an intervention[2].

HIV state	Rural context		Urban context	
PMTCT	Base case value (BCV)	Evidence base	Base case Value (BCV)	Evidence base
Non-infected Infected with no AIDS AIDS Deaths	0.90 0.67 0.30 0	[46] , [47], [48] [46], [47], [48] [46], [47], [48] [46], [47],[48]	0.95 0.75 0.65 0	[46], [47],[48] [46], [47],[48] [46], [47],[48] [46], [47],[48]
HAART FOR DULTS	BCV	Evidence base	BCV	Evidence base
Non-AIDS AIDS Deaths	0.67 0.55 0	[46] , [47], [48] [46], [47], [48] [46], [47], [48]	0.90 0.70 0	[46], [47],[48] [46], [47],[48] [46], [47],[48]
HAART FOR CHILDREN	BCV	Evidence base	BCV	Evidence base
Non-AIDS AIDS Death	0.67 0.50 0	[46] , [47], [48] [46], [47], [48] [46], [47], [48]	0.80 0.70 0	[46], [47],[48] [46], [47],[48] [46], [47],[48]

To get the costs, health outcomes in subsequent three-month Markov periods, the baseline cost and quality of life are applied to changing transition probabilities. Changes in transition probabilities in HIV/AIDS state over time in successive three-month Markov period is pegged on the trends suggested by the projections by Spectrum Policy Modeling systems [32] which is a separate model used to models interactions between area and each HIV/AIDS intervention.

The total costs health outcomes are discounted at 3% discounted rate as per cost-effectiveness expert recommendations [49]. Given that South African government is the main funder of HIV/AIDS interventions, the costs are evaluated from government perspective although results of the societal perspective are also shown for the sake of comparison with studies elsewhere. Average estimates of waiting time, transport costs and funeral costs are added to the cost of the government perspective to determine the costs of the societal perspective. Real costs are also considered using 2007 as the base-year. Probabilistic sensitivity analysis is finally conducted to take into account the uncertainty underlying the analyses. All these analyses are conducted using TreeAge Pro

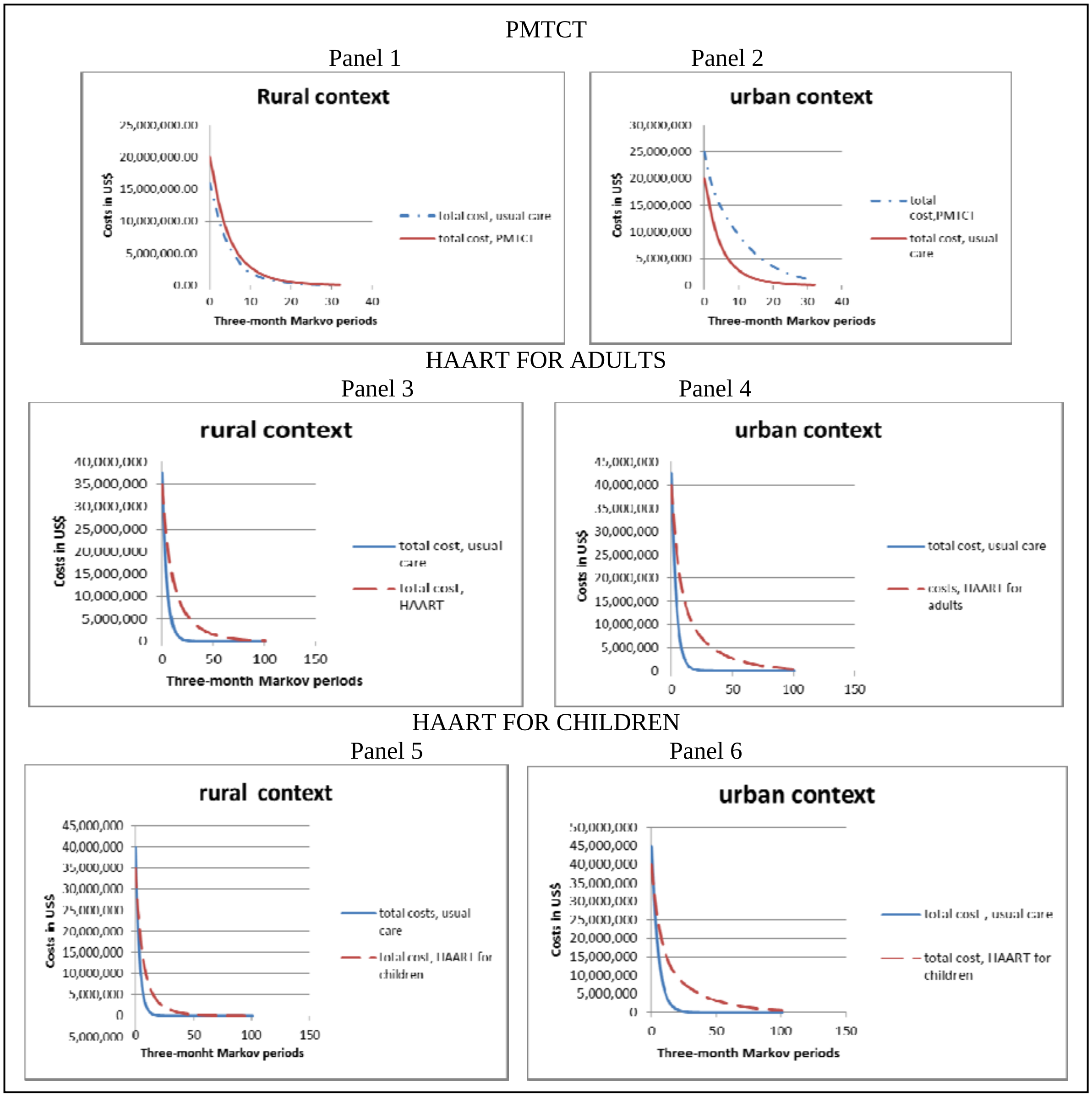
[2] The quality of life data were obtained from quality of life studies in South Africa ([46],[47],[48]). The quality of life in a. rural context was approximated with the average quality of life of people who live predominantly a rural context, the black population. Similarly, the quality of life for the urban context was estimated on basis of the average quality of life for the white population

and are presented next.

II. RESULTS

A. *Relative costs*

The relative costs of HIV/AIDS interventions in rural and urban areas of South Africa are presented first. Figure 1 depicts the graphical analysis of such costs (Note that in the figure the word context is used while the text talks about area. In this paper area and context are considered conceptually equivalent.)



Source: Author, based on the results of Markov models' simulations.

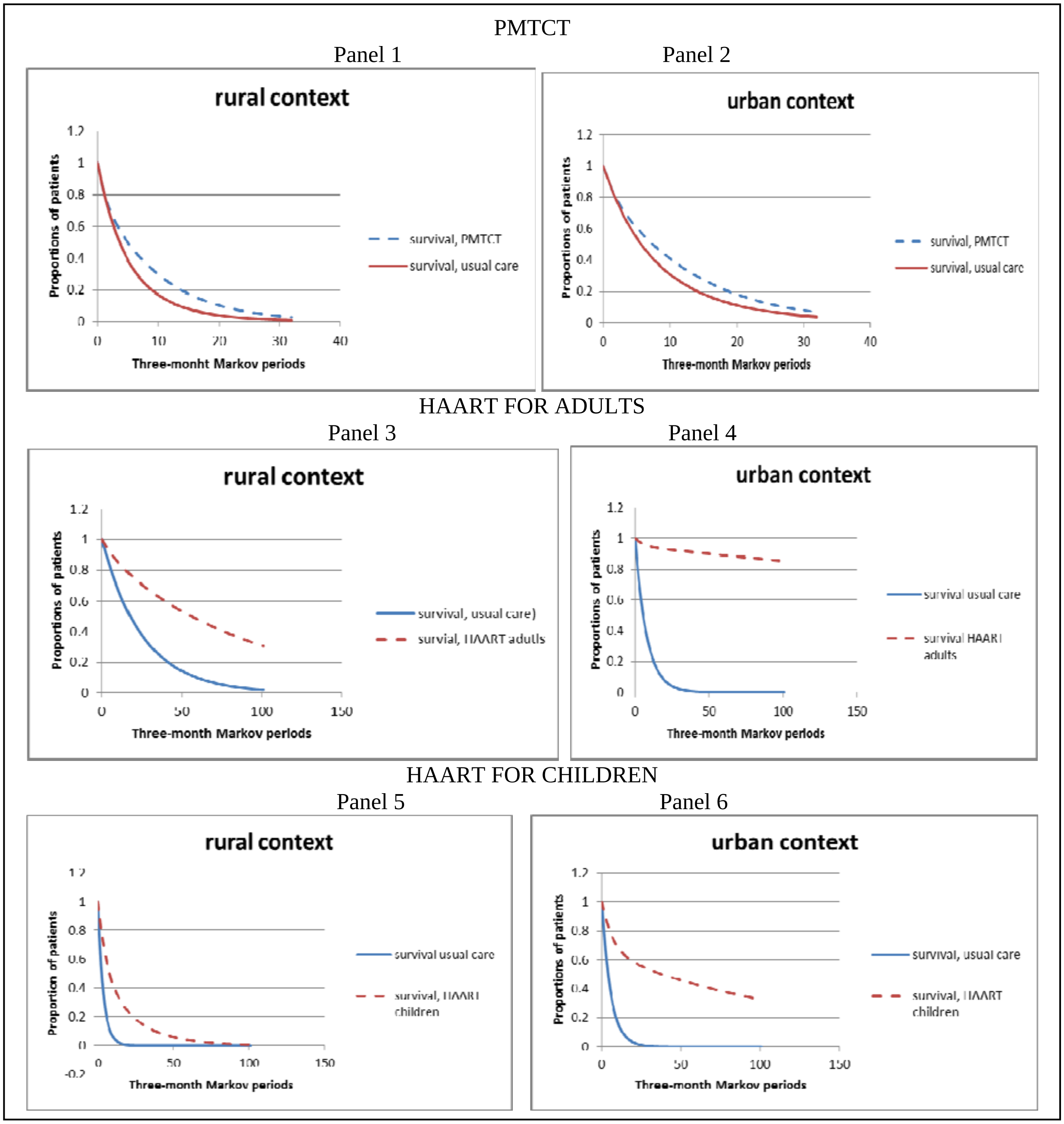
Figure: 1 Overall comparison of the lifetime cost of HIV/AIDS interventions across a rural area and an urban area (in US$, government perspective)

The figure depicts that the cost of HIV/AIDS interventions over time are lower in a rural area than they are in an urban area of South Africa. The Figure shows for example that at period 10 of Markov model, PMTCT costs about a third of US$5,000,000 in a rural area while at the same period it costs about US $10,000,000. At period 10, the cost of USUAL CARE related to PMTCT is about a third of US$ 5,000,000 in a rural area while it is about half of US$5, 000,000 in the urban area. The results for other intervention present similar patterns although the differences between the costs of USUAL CARE related to HAART interventions in a rural area and the costs of USUAL CARE related to HAART interventions an urban area are not different. Given that the model assumes a same size of hypothetical patients in each area, it can be concluded that the costs of HIV/AIDS interventions are relatively lower in a rural area than they are in an urban area.

Analyzing relative costs in terms of the difference in costs between an HIV/AIDS interventions and its related usual care, Figure 1 shows that the gap between USUAL CARE and an HIV/AIDS intervention is lower in rural area than it is an urban area (Panel 1 to 6). This result suggests that in relation to USUAL CARE, an HIV/AIDS intervention in a rural area, add less costs to already existing costs of USUAL CARE. In other words, relative to USUAL CARE, an HIV/AIDS intervention in an urban area results in more incremental costs relatively to the incremental costs in a rural area. The next section discusses effectiveness.

B. Relative effectiveness

Defining the effectiveness as additional health outcomes of an intervention relative to health outcomes of a given situation, the effectiveness of an HIV/AIDS intervention in a rural area is analysed relative to health outcomes in an urban area while the effectiveness of an HIV/AIDS intervention in a given area, is analysed relative to health outcomes of USUAL CARE. The effectiveness analysis starts with survival as health outcomes and then move on to survival adjusted with quality of life. The results of survival in rural and urban areas are presented in Figure 2.



Source: Author, based on the results of Markov models' simulations.

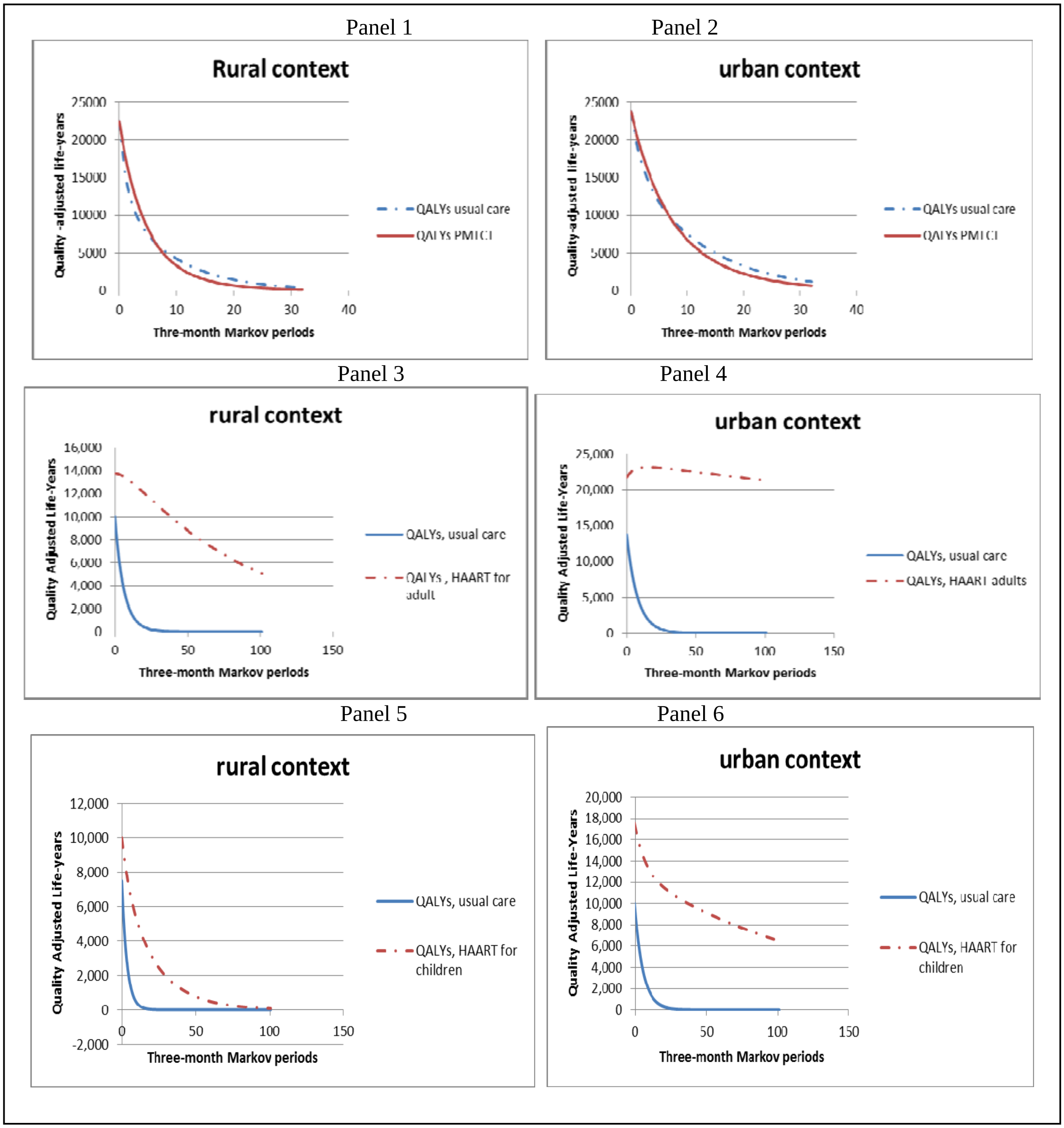
Figure 2: Comparison of HIV/AIDS interventions-induced survival in rural urban areas.

Figure 2 shows that the patterns of survival over time in rural and urban areas in South Africa are different for both HIV/AIDS interventions and related USUAL CARE. Specifically, survival is generally lower in a rural area than it is in an urban area. The figure shows for example that at Markov period 10, 26% of the cohort using PMTCT survives in rural area while the corresponding figure for the urban area is 40%. At the same period, survival with USUAL CARE in a rural area is 18% while survival in an urban area is about 26%. It is to note however that while survival under HAART is clearly lower in a rural area than it is in an urban area, the patterns of survival under HAART-related USUAL CARE is not clearly different in a rural area and an urban area. At Markov period 50 for example, survival under HAART FOR ADULTS-related USUAL CARE is about 40% in a rural area while it is about 0% an urban area although earlier at Markov period 10, survival under HAART–related USUAL CARE is consistent with patterns of survival for HIV/AIDS interventions. These results indicate that under USUAL CARE, a proportion of patients resisting the epidemic in the rural area might be greater than the proportion of patients resisting the epidemic in an urban area.

Comparing survival in each area, Figure 2 shows that, as expected, survival in USUAL CARE is less than survival under related HIV/AIDS interventions regardless of the area. For instance in a rural area, Figure 2, Panel 3 shows that at period 10, survival under USUAL CARE is about 15% while it is about 50% under related HAART intervention. Similarly in an urban area, Panel 6 of the figure show for instance that at period 50, survival under USUAL CARE is about 0% while it is about 48% in related HAART interventions.

The paper is more interested in the comparison of additional survival (incremental effectiveness) of an HIV/AIDS intervention across a rural area and an urban area. The incremental effectiveness is graphically shown by the gap between the USUAL CARE survival curve and a given HIV/AIDS survival curve. The results in Figure 2 suggest that PMTCT is relatively more effective in a rural area on the basis of the gap between the PMTCT survival curve and USUAL CARE survival curve, although the difference in the gap across area is not that much (Panel 1 and panel 2). While the gap difference between PMTCT and USUAL CARE curves across a rural and an urban area is almost insignificant, the gap is significant with HAART FOR ADULTS and HAART FOR CHILDREN (Panel 3 and Panel 4, Panel 5 and Panel 6). The results show that HAART FOR ADULTS and HAART FOR CHILDREN are relatively less effective in a rural area than they are in an urban area on the basis of the gap between survival curves for the two interventions and USUAL CARE

Figure 2 has compared relative effectiveness of HIV/AIDS interventions across a rural area and an urban area using survival as a measure of health outcome. Survival may not be an accurate measure of health status because long survival can prevail in poor health conditions than short survival such that overall, taking into account quality of life, short survival might results in greater health outcomes. Discounting also makes QALYs gained during later periods of modeling worth less than QALYs gained in earlier periods Therefore, this paper produced survival (life-years) by multiplying the size of hypothetical cohort with proportions of patients surviving in each HIV/AIDS state of a Markov period. The result was then multiplied with the quality of life to produce quality-adjusted life-years (QALYs) at each period. The results are illustrated in Figure 3.



Source: Author, based on the results of Markov models' simulations.
Figure 3 Comparison of HIV/AIDS interventions-induced QALYs across rural and urban areas.

As Figure 3 shows, except for PMTCT (Panel 1 and Panel 2), the results in terms of QALYs appear to be consistent with the results for survival (Panel 3 and Panel 4, Panel 5 and Panel 6). The results show that, in relation to USUAL CARE, HIV/AIDS interventions are generally more effective in the urban area than in the rural area when survival (life-years) are adjusted for the quality of life (QALYs) are used as measures of effectiveness.

C. Relative cost-effectiveness

A good grasp of the relative performance of an HIV/AIDS intervention in rural and urban areas requires ultimately the joint analysis of cost and effectiveness. The numerical results of such analysis are in Table 4.

Table 4 Lifetime cost (US$), effectiveness (QALYs) and Cost-effectiveness (US$/QALY) for a cohort of 100,000 patients

Intervention	Rural area	Urban area	Value in a rural area as a % of the value in the urban area
USUAL CARE			
Total costs (GP)	146,700,000	319,400,000	46
Total costs (SP)	153,146,300	352,425,326	46
Total effectiveness (QALYs)	517,151	765,745	67
PMTCT			
Total cost (GP)	156,526,596	353,294,195	44
Total cost (SP)	162,589,125	361,152,326	43
Total effectiveness	580,142	884,672	65
Incremental cost	***9,826,596***	***33,894,195***	***29***
Incremental effectiveness (QALYs)	***62,991***	***118,927***	***53***
ICER (GP)	***156***	***285***	***54***
ICER (SP)	***167***	***301***	***61***
USUAL CARE			
Total costs (GP)	245,572,741	382,345,997	64
Total cost (SP)	251,156,256	390,126,326	63
Total effectiveness	1,955,943	2,178,923	89
HAART FOR ADULTS			
Total cost	858,139,181	952,828,151	89
Total effectiveness	2,088,378	3,186,842	65
Incremental cost	***612,566,440***	***570,482,154***	***107***
Incremental effectiveness (QALYs)	***715,615***	***1,007,919***	***70***
ICER (GP)	***856***	***566***	***151***
ICER (SP)	***899***	***573***	***151***
USUAL CARE			
Total costs	154,438,775	265,539,917	58
Total effectiveness	1,267,170	1,575,734	80
HAART FOR ADULTS			
Total cost GP	474,564,909	443,906,801	35
Total cost SP	482,546,312	450,123,156	36
Total effectiveness	2,109,841	2,547,809	82
Incremental cost	***320,126,134***	***178,366,884***	***179***
Incremental effectiveness (QALYs)	***842,671***	***972,075***	***86***
ICER (GP)	***985***	***650***	***151***
ICER (SP)	***995***	***656***	***153***

Source: Author, based on the results of Markov models' simulations.

The results in the Table as to how the costs of an HIV/AIDS intervention compare across areas or howeffectiveness of an HIV/AIDS intervention compare to those of USUAL CARE is consistent with graphical analysis. In the analysis that follows, the paper focus on the comparison, across areas, of incremental costs, effectiveness, and cost-effectiveness of an intervention relative to USUAL CARE

As for the incremental costs, Table 4 shows the incremental cost (IC) of PMTCT in the rural area is less than the IC of PMTCT in the urban area. The IC of PMTCT in a rural area represents 29% of its IC in the urban area. However, the opposite is true for HAART FOR ADULTS and HAART FOR CHILDREN whose incremental costs in a rural area represent 107% and 179% of their respective incremental cost in an urban area. These results indicate that the patterns of incremental costs of HIV/AIDS interventions relative to USUAL CARE across a rural area and an urban area are not the same.

While the pattern of incremental costs across a rural area and an urban area is different across HIV/AIDS interventions, the opposite is true for the incremental effectiveness. Table 4 shows that, the incremental effectiveness of an HIV/AIDS intervention is generally lower in a rural area than it is in an urban area. For example, the incremental effectiveness of PMTCT in a rural area is 53% of its incremental effectiveness in an urban area. The corresponding figures for HAART for adults and HAART for children are 107% and 179%. These results show that HIV/AIDS interventions are less effective in a rural area than in an urban one.

Table 4 further shows that the ICER of PMTCT in a rural area is lower than its ICER in an urban area. Since ICER means cost per effectiveness, a lower ICER for PMTCT in a rural area means that PMTCT is more cost-effective in the rural area than it is in an urban area. While the results show that PMTCT is more cost-effective in a rural area than it is in an urban area, they show that HAART FOR ADULTS and HAART FOR CHILDREN have greater ICERs in a rural area, indicating that they are less cost-effective in this area than they are in an urban area. These results indicate that there is no specific pattern of CE across areas common to all modeled HIV/AIDS interventions.

The fact that HAART is less cost-effective in a rural area can be explained by a number of reasons. First, HAART may be adding more to the costs of USUAL CARE than it adds to the effectiveness of USUAL CARE in the rural area, resulting in greater ICER in the rural area. Alternatively, HAART may be adding less to the costs of USUAL CARE than it adds to the effectiveness of USUAL CARE in an urban area.

Defining the equality of the CE of an HIV/AIDS intervention across areas as the equality of the ICERs of that intervention across these areas, this implies that in case of such equality the ICER value in Column 3 of Table 4 would be 100. The results in Table 4 show that the ICER value in column 3 varies to a greater extent around 100. Measuring the extent of CE of an intervention across a rural area and an urban area as the distance the ICER value is far away from 100, the extent of CE of modeled interventions becomes clear from Table 5.

Table 5: Summary comparison of cost-effectiveness of HIV/AIDS interventions in a rural area and an urban area (in US$/outcome)

Intervention	ICER in a rural area	ICER in an urban area	ICER in a rural area as % of the ICER in an urban area
PMTCT	156	285	54
HAART FOR ADULTS	856	566	151
HAART FOR CHILDREN	985	650	151

Source: Author, based on the results of Markov models' simulations.

Table 5 shows indeed that the extent of CE of HIV/AIDS interventions is different. The table shows that HAART interventions are less cost-effective in the rural area than they are in the urban area. Their ICER relative to USUAL CARE in the rural area is greater than their ICER relative to USUAL CARE in the urban area. These ICERs in the rural area represent 151% of the ICERs in the urban area. In contrast, PMTCT is more cost-effective in a rural area. Its ICER relative to USUAL CARE in a rural area is less than its ICER in an urban area to the extent that the ICER in the rural area represents 54% of the ICER in the urban area.

In summary, the results presented in Table 5 suggest that there is no specific trend in CE from a rural area to an urban area for modeled HIV/AIDS interventions. Furthermore, the results show different extent of CE across HIV/AIDS interventions. These results were subjected to probabilistic sensitivity analysis. Table 6 presents the results of such analysis.

Table 6: Results of probabilistic sensitivity analysis assuming no 2010 guidelines (US$, 3% discount rate, Government's perspective***)***

	Average rural area		Average urban area	
Intervention	Cost ($)	(QALYs)	Costs ($)	QALYs
PMTCT USUAL CARE 95% CI	955 (833-3019)	8 (5-11)	2483 (1799-4593)	8 (6-13)
PMTCT 95% CI	1627 (187-1785)	12 (5-15)	3311 (1527-3504)	11 (6-16)
ICER	168		276	

HAART FOR ADULT USUAL CARE 95% CI	2909 (2709-3114)	17 (6-33)	3822 (3627-4027)	6 (4-9)
HAART FOR ADUTLS	9909 (6821-13507)	19 (8-28)	17310 (6697-18497)	30 (17-42)
95% CI ICER	875		562	Per cent=1353
HAART FOR CHILDREN USUAL CARE 95% CI	1543 (1355-1729)	4 (3-5)	2664 (2471-2853)	5 (4-6)
HAART FOR CHILDREN	5375 (3376-6756)	8 (5-11)	10,440 (4248-14633)	17 (9-25)
ICER	958		648	

Source: Author, based on the results of Markov models' simulations.

The results of the probabilistic sensitivity analysis in Table 6 show that the conclusions of the base-case analysis do not change. They are, however, based on the evidence for the guidelines before 2010. Further sensitivity analysis is conducted to check the comparability of the interventions across areas with the implementation of the 2010 guidelines. Following the guidelines for PMTCT and HAART issued in 2010 South Africa adopted earlier HAART treatment in 2011. Incorporating the available evidence on earlier treatment and earlier PMTCT in base-case values and conducting probabilistic sensitivity analysis, the results are reported in Table 7.

Table 7 Results of probabilistic sensitivity analysis with 2010 guidelines (3% discount rate, GP)

	Average rural area		Average urban area	
Intervention	Cost ($)	(QALYs)	Costs ($)	QALYs
PMTCT USUAL CARE 95% CI	1948 (833-3019)	8 (5-11)	3192 (1799-4593)	8 (6-13)
PMTCT 95% CI	2244 (255-2723)	10 (5-13)	3700 (1588-4497)	10 (7-14)
ICER	148		254	
USUAL CARE 95% CI	2909 (2709-3114)	17 (6-33)	3822 (3627-4027)	6 (4-9)
HAART for adults 95% CI	5264 (4325-10987)	20 (7-23)	15222 (6401-18350)	31 (18-43)
ICER	785		456	

Source: Author, based on the results of Markov models' simulations

With earlier implementation of PMTCT and HAART, the cost per QALY gained decreases. However this does not affect the comparability of each intervention across areas.

III. DISCUSSION OF THE RESULTS

The results in this paper have shown that the ICER of all modeled HIV/AIDS interventions across a rural area and an urban area are different. This is illustrated by the fact that the ICER of an HIV/AIDS intervention in a rural area as a percentage of the ICER in an urban area is not 100%. This result suggests that HIV/AIDS interventions are not equally cost-effective across a rural area and an urban area.

The results have also shown that the trends in CE across a rural area and an urban area are not the same. The ICER of PMTCT was lower in the rural area than it was in the urban area while the ICERs of HAART FOR ADULTS and HAART FOR CHILDREN were greater in the rural area than they were in an urban area. This result indicates an absence of consistent trends in the CE of HIV/AIDS interventions across a rural area and an urban area. A trend would exist if the ICER of each HIV/AIDS intervention in a rural area as a percentage of the ICER in the urban area is consistently lower or greater than 100%.

Further to the lack of consistent trends in CE of HIV/AIDS interventions across a rural area and an urban area, it was observed that the extent to which the ICER of an HIV/AIDS intervention in a rural area as % of its ICER deviated from 100% was different across interventions. The ICER of PMTCT in a rural area as a percentage of its ICER in an urban area was 54% while the corresponding percentages for HAART FOR ADULTS and HAART FOR CHILDREN were 151%. The fact that the ICERs in a rural area as a percentage of the ICERs in an urban area is farther away from 100% for HAART FOR ADULTS and HAART FOR CHILDREN than it is for PMTCT, indicates that the extent of CE across modeled HIV/AIDS interventions is not the same. With the ICER meaning the additional costs per health outcome, a lower ICER in a given area implies more cost-effectiveness. The evidence shows that PMTCT is more cost-effective in the rural area than it is in an urban area. By contrast, HAART FOR ADULTS and HAART FOR CHILDREN are less cost-effective in a rural area since their ICERs in this area represent 151% and 151%, respectively of their ICERs in an urban area.

An initial question was whether or not comparing the CE of HIV/AIDS interventions across a rural area and an urban area would result in different CE results. This question is answered by these results. Indeed, the results presented in this chapter have shown that the CE of HIV/AIDS intervention depends on areas. However, bearing in mind the design of CE in this chapter, the results are expected to be similar. In fact, in each area, the CE of an intervention was analyzed on the same size cohort of patients, starting in the same HIV/AIDS state. The fact that the CE was shown to be different is at the centre of the rationale for this comparison. One would have expected the cost of interventions to be lower in an urban area. Better living standard in the urban area are expected to cushion the degradation of health status as result of HIV/AIDS, reduce the need to seek care and consequently reduced the costs of intervention over time. The higher costs in an urban area may in this case be explained by higher levels of usage of health care in an urban area.

The comparison of HIV/AIDS interventions was grounded on the fact that the outcomes of HIV/AIDS interventions, particularly the CE, are a result of the interaction between area, individual patients and the intervention. These factors, which have been theorized differently in the literature, are expected to prevail differently across a rural area and an urban area both in terms of trends and extent. In turn, these differences may influence the outcomes of interventions especially when one acknowledges that HIV/AIDS interventions do not necessarily target all contextual and individual factors. Due to the fact that the analysis took these interactions into account by pegging the progression of patients in HIV/AIDS states over time to projections of Spectrum Policy Modeling System, these results were expected, although there was no indication as to the trends and extent of CE across a rural area and an urban area or across HIV/AIDS interventions.

The observed extent of CE across HIV/AIDS interventions can be explained using the components of cost-effectiveness. The fact that PMTCT was more cost-effective in the rural area means that, relative to USUAL CARE, it achieves relatively more effectiveness given additional costs in the rural area compared with the urban area. Since PMTCT is conducted with pregnant women who use primary health care facilities in both rural and urban areas, it is likely that the risk of infection is detected and prevented. By contrast, with low HIV screening rates, the impact of the epidemic is detected too late when health status has deteriorated. In the case of an urban area, better living conditions can cushion the impact, resulting in HAART interventions being relatively more effective in the urban area than in the rural area.

Other studies have found that HIV/AIDS interventions have generally produced better effectiveness results in better socio-economic contexts,[50] for example. However, the rate of infections has been smaller in lower socio-economic areas in developing countries [51]. This supports the finding that, depending on the underlying factors, different outcomes of HIV/AIDS interventions can be observed. In a nutshell, one can conclude that the CE of HIV/AIDS interventions depends on the area. This conclusion has implications for South African policy makers. Policy makers, who have been allocating resources based on other considerations, could include considerations of CE of HIV/AIDS interventions in socio-economic contexts to improve the efficiency of such HIV/AIDS interventions and so allocate their limited resources to the best effect.

Finally, the results of this study need to be considered with care in light of the cost and effectiveness evidence used. The cost and effectiveness data have limitations and the results may suffer in terms of accuracy. Despite these drawbacks, the study addressed the issue of uncertainty in order to ensure that the findings of the study will be of value to policy makers in South Africa.

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