Cost-effectiveness analysis of combined antiretroviral therapy in a tertiary health institution

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ABSTRACT

Background: The increasing health care spending from government, donors and private stand-point has a lot of challenge in health care related decision making. Hence, there is need to examine closely the cost and benefits of drug interventions especially in chronic illnesses like HIV/AIDS.

Objective: To conduct cost-effectiveness analysis of combined antiretroviral therapy (cART) in a tertiary health institution

Methods: A retrospective review of systematically sampled 360 case notes was conducted. World Health Organization Defined Daily Dose method of evaluating drug use and probability method for potential effectiveness of cART options from literature analysis was employed in determining cost-effectiveness of each option identified from cART drug utilization studies.

Results: Zidovudine (AZT)+Lamivudine (3TC) +Nevirapine (NVP)which cost N89 ($ 0.3 per unit effectiveness) was more frequently prescribed (86%, ^{2}=100.82; P=0.00; df=1). This combination was more cost effective than the less frequently prescribed first line option of Tenofovir (TDF) +Lamivudine (3TC) +Efavirenz (EFV)at a cost per unit effectiveness of NGN 134 ($0.45).Similarly, AZT+3TC+Lopinavir/Ritonavir (LPV/r)which was more frequently prescribed (71.4%, ^{2}=33.62; P=0.00; df=1)]with cost per unit effectiveness of NGN379 ($1.26)was more cost effective than TDF+3TC+LPV/r [NGN403($ 1.34) per unit of effectiveness] in the management of HIV/AIDS patients as second line regimen.

Conclusions: AZT+3TC+NVPwas more cost-effective than TDF+3TC+EFV in the management of HIV/AIDS patients as firstline regimen. However, AZT+3TC+LPV/r appeared to, but was not necessarily more cost effective than TDF+3TC+LPV/r in the management of HIV/AIDS patients as second line regimen.

Keywords: Cost-Effectiveness analysis, cART, HIV/AIDS, Defined Daily Dose.

Analyse coût-efficacité de la thérapie antirétrovirale combinée dans un centre hospitalier

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RÉSUMÉ

Contexte: L'augmentation des dépenses en soins de santé du gouvernement, des donateurs et du secteur privé présente beaucoup de défis dans la prise de décisions liées aux soins de santé. Par conséquent, il est nécessaire d'examiner de près les coûts et les avantages des interventions à base de médicaments, en particulier dans les maladies chroniques comme le VIH/sida.

Objectif: Effectuer une analyse coût-efficacité de la thérapie antirétrovirale (ARV) combinée dans un centre hospitalier.

Méthodes: un examen rétrospectif des 360 cas systématiquement échantillonnés a été effectué. La méthode de dose journalière d'évaluation de l'usage de médicaments définie par l'Organisation mondiale de la santé et la méthode de probabilité pour l'efficacité potentielle des options de thérapie antirétrovirale combinée à partir de l'analyse de la littérature a été utilisée pour déterminer la rentabilité de chaque option identifiée à partir des études sur l'utilisation de médicaments dans la thérapie antirétrovirale combinée.

Résultats: La combinaison Zidovudine (AZT)+Lamivudine (3TC)+Névirapine (NVP) qui a coûté N89 ($0,3 par unité d'efficacité) était plus fréquemment prescrite (86%, ^{2} = 100,82; P=0,00; df=1). Cette combinaison était plus rentable que l'option de première ligne la moins fréquemment prescrite de la Ténofovir (TDF)+Lamivudine (3TC)+Efavirenz (EFV) à un coût par unité d'efficacité de NGN 134 ($0,45). De même, l'AZT+3TC+Lopinavir/Ritonavir (LPV/r) qui était plus fréquemment prescrit (71,4%, ^{2}=33,62; P=0,00; df=1)] avec le coût par unité d'efficacité de NGN379 (1,26 $) a été plus rentable que TDF+3TC+LPV/r [NGN403 ($1,34) par unité d'efficacité] dans la gestion des patients VIH/sida comme régime de deuxième ligne.

Conclusions: AZT+3TC+NVP était plus rentable que TDF+3TC+EFV dans la gestion des patients VIH/sida comme régime de première ligne. Toutefois, l'AZT+3TC+LPV/r est apparu, mais n'était pas nécessairement plus rentable que TDF+3TC+LPV/r dans la gestion des patients VIH/sida comme régime de deuxième ligne.

Mots-clés: analyse coût-efficacité, thérapie antirétrovirale combinée, VIH/sida, dose quotidienne définie.

INTRODUCTION

Health care spending is increasing, both from government, donors and private stand-point.[1] Pharmacy practitioners and managers face a multitude of economic challenges in health related decision making. The impact of cost containment is causing administrators and policy makers in pharmacy to examine closely the cost and benefits of both proposed and existing interventions.[2] Private employers and donor agencies are demanding that health problems be evaluated in terms of clinical and social outcomes related to the cost incurred.[3] Pharmaco-economic approach can be used to analyze the value of health services to the public, as opposed to the traditional market place scenario where values are measured by the prices that the patient or patron is willing to pay. The use of valid economic evaluation methods to measure the value and impact of new services can increase acceptance of such programs by the medical profession, third party payers and consumers.[4,5,6]

Moreover, with the depressing nature of economy in many countries such as Nigeria where per capita income is low, there is need for utmost consideration for cost containment measures. The healthcare environment is clearly in a state of rapid evolution. Traditional approach to health care decisions will no longer suffice; therefore, new tools would be required. Medical, ethical and societal concerns about costs, access and quality of care are making healthcare practitioners to consider more comprehensive model for medical decisions. Consequently, interest in research to assess outcomes of healthcare has been increasing. These trends have led to the evolution of pharmaco-economics: a relatively new discipline in pharmacy.[7] Pharmaco-economics has been defined as the description and analysis of cost of drug therapy to health care system and society.[7] It is a specialized aspect of health economics which involves the use of economic principles and techniques of analysis to ensure that scarce healthcare resources are used more efficiently.[8] The objective of pharmaco-economic study is to influence policy formulation and effect decision making, that is to make a person or a group of people change their behaviour and persuade them that a new course of action is a “better” one, “better” simply means that in economic terms, it is more efficient.[8]

Human Immuno-Deficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) is a chronic, incurable condition. At the end of 2007, 33 million people were estimated to be living with HIV and 2.7 million became newly infected while 2 million died from the disease. About 68% of persons infected reside in Sub-Saharan Africa.[9] WHO accorded priority status to HIV/AIDS.However,many public health planners remain largely unaware of its magnitude and the seriousness of its complications. Of equal consequence is the increasing prevalence of the disease and the long-term cost of therapy to patients, donors and the health sector, and its cost to nations in economic terms due to the fact that use of antiretroviral drugs in the management of HIV/AIDS is for lifetime of the patients from time of diagnosis. This translates into a substantial cost in drug therapy to the patients, government and donor agencies.[9] HIV/AIDS is of public health importance particularly as it has no known cure. The prevalence is increasing with a wide range of complications that have clinical, social and economic implications. Upon consideration of the impact of antiretroviral therapy on the overall cost of healthcare of HIV/AIDS patients who uses this class of drugs for lifetime from time of diagnosis, effort designed to reduce expenditure on this class of drugs as well as using them more effectively would be advantageous. This group of patients also faced with the problem of drug availability, affordability and resistance (especially when adherence is not up to 98%).HIV/AIDS, if not adequately managed, can result in a wide range of complications that have clinical, social and economic implications.[10] A form of anti-retroviral drugs utilization study and consequently their economic evaluation is needed to promote rational antiretroviral drugs prescribing and improve economic, clinical and humanistic outcome of antiretroviral therapy.[11] For this reasons, subjecting identified options of combined Active Antiretroviral Therapy (cART) to pharmaco-economic evaluationis very paramount. More so related studies are scarce in literature.

The study was therefore designed to conduct cost-effectiveness analysis of the various cART options in UITH in Patients with HIV/AIDS, which can promote rational decision on choice of drugs.

METHODS

Setting

The study was conducted at the University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State, Nigeria. The Hospital was chosen because it was the only University Teaching Hospital in Kwara state and the major HIV/AIDS referral center in the state.

The bed complements for the hospital were 1,613 as at January, 2016. About 50 registered pharmacists were in the employment of the Hospital. The Hospital runs a medical out-patient department comprising of a

general out-patient and specialist medical out-patient clinics. The cART clinic is one of the specialist medical out-patient clinics and it is run, every Monday to Friday with average monthly turnover of 120 patients.

Study Population and Sample Size

HIV/AIDS patients that were registered with and attended the cART clinic of UITH were the subjects for the study. Their population was obtained from Medical Record Department. totaling 4,800. Fischer's Formula was applied to determine sample size from this estimate.[12] The required minimum sample size was 360.

Inclusion Criteria were HIV/AIDS out-patient registered with UITH cART clinic regardless of sex and concurrent illness, HIV/AIDS patients that have been on drug therapy for at least one year and adult of 18 years and above.

However, HIV/AIDS in-patients and HIV/AIDS patients below 18 years were excluded from this study.

Study Design

Ethical approval was obtained from Research and Ethics Committee of UITH.

The study is a retrospective cross sectional review of old and new cases of cART among HIV/AIDS patients. Systematic random sampling method was adopted using sampling interval of 5 for case notes from Medical Records department. In all, a total of 360 case notes were sampled. Standard cost accounting technique was adopted in cost computation.

Treatment Options

Drug utilization pattern of the various treatment options available (First and Second Lines of cART) as identified from case-notes of the subjects was carried out.

Economic Perspective

Economic perspective of the donor agencies and the Hospital was considered since the drug, diagnostic and monitoring tests, care and support costs, including transport cost were borne by the agencies while personnel costs were borne by the Hospital Management.

Data Instrument

Data was collected using a pre-tested, standardized data collection form.. It has columns for Code Number as the Patient's Hospital Number, date of visit, demographic data, concurrent illness (s), CD4 cells count, weight, concurrent illness', drugs prescribed with duration at each visit and cost, diagnostic/monitoring tests, transport cost, duration of present regimen(month), physicians remark on CD4 cells count, as well as defined daily dose of each regimen and their respective costs.

A standardized effectiveness rating format and decision analysis tables were used to document, rate and analyze effectiveness criteria of anti-retroviral drugs generated from literature.

Data Collection

Patients were coded using their respective hospital number.Anti-retroviral drugs prescriptions were filled into the data collection form from information extracted from case notes.Other relevant information, such as serial number, CD4 cells count at diagnosis, weight in (kg) at diagnosis, relevant diagnostic/ monitoring tests, concurrent illness, prescriptions (generic &branded), duration of present regimen,(month),physicians remark on CD4 cells count, defined daily dose, cost/defined daily dose.

Cost Measure

In this study, only drug cost was considered. Dispensing and transport costs were assumed to be the same for all the treatment options identified.

Antiretroviral therapy is a lifelong management but follow up visit to the physician is usually every three months (90 days). Total Cost of a Treatment Option = Mean Cost per Defined Daily Dosage (DDD) x Duration of Therapy.

Mean cost/DDD of treatment options available at UITH was used.

Effectiveness (Outcome) Measure

The effectiveness measure involved theoretical framework by analysis of positive and negative outcome of each treatment option from review of literature to establish probabilities of the outcomes and applying decision analysis for effectiveness.[13]

Effectiveness of a treatment option (in natural unit) = Sum of all criterion rating. Criterion Rating = Criterion Value X Assigned Weight.

The criterion value and assigned weight which determines the criterion rating is somewhat arbitrary hence fairly subjective. However, each option being considered was treated identically with respect to the assigned weight to limit the subjectivity.

More so, the value given to each characteristic (criterion) is determined by decision-maker(s) who will make use of the result of analysis in taking decision.[13]

Criterion values were obtained from analysis of positive and negative outcome of different criteria (characteristics) of a treatment option from review of literature in natural unit[3]. For example, criteria for Anti-Retroviral drugs effectiveness (outcome) and respective assigned weight include Efficacy (0.3),Tolerability (0.2), Daily Pill burden (0.1),Food Interactions (0.2) and Safety of Administration (0.2).

Hypothesis

There is no significant difference in the effectiveness of cART Options available for management of HIV/AIDS

Cost Effectiveness Analysis (CEA)

Cost Effectiveness Analysis indicates which intervention provides the highest "value for money" and helps to choose the intervention which maximizes health for the available resources .[14]

Cost Effectiveness Analysis was carried out by calculating:

i) The cost i.e. the resources required to implement an intervention.

ii) The effectiveness i.e. the extent to which current and potential interventions improves population health. It is otherwise known as outcome.

$$CEA = \frac{\text{Total cost of a treatment option (in monetary unit)}}{\text{Effectiveness of the treatment option (in natural unit)}} = C/E$$

[14,15]

This was determined and compared for available options in each stage of cART

Sensitivity Analysis

Sensitivity Analysis was performed to test whether the decisions changes when specific variables (e.g. cost, effectiveness) were altered within reasonable range (10-25%) in favour of less cost-effective option.

Data Analysis

The collected data was analyzed using EPI- INFO software version 3.4.1 2007. Data was presented as frequency distribution tables. Chi-Square analysis was used to compare proportions and hypothesis testing. P -values < 0.05 were considered significant.

RESULTS

Anti-Retroviral Drug Utilization/Identified Treatment Options for Cost Effectiveness Analysis

Three hundred and fifty three (98.1%) of the 360 subjects were on first line therapy while the remaining 7 (1.8%) were on second line therapy.

Three hundred and four (86.1%) subjects out of the 353 on first line therapy took AZT+3TC+NVP while the remaining 49 (13.9%) took TDF+3TC+EFV. There was statistically significant difference between these proportions (^{2}=100.82; P=0.00; df=1).

Five (71.4%) subjects out of the 7 on second line therapy took AZT+3TC+LPV/r while the remaining 2 (28.6%) took TDF+3TC+LPV/r. There was statistically significant difference between these proportions (^{2}=33.62; P=0.00; df=1).

Effectiveness Rating of Therapeutic Options in First line Antiretroviral Regimen

The values for effectiveness rating of antiretroviral drugs from review of literature [16,17,18] were 75% (efficacy), 50% (daily pill burden), 64%(tolerability), 100%(food interaction) for AZT+3TC+NVP and 77% (efficacy), 50% (daily pill burden), 56%(tolerability), 40%(food interaction) for TDF+3TC+EFV in the first line antiretroviral regimen. The details are as shown in Table 1.

Table1: Effectiveness Rating of Therapeutic Options in first line Antiretroviral Regimen

Criteria	Option I: AZT+3TC+NVP	Value	Option II: TDF+3TC+EFV	Value
1. Efficacy	AZT: 75% 3TC: 80% NVP: 70% **Mean: 75%**	75%	TDF: 81% 3TC: 80% EFV: 70% **Mean: 77%**	77%
2. Daily Pill Burden	AZT+3TC+NVP: **2 tablets per day**	50%	TDF+3TC: 1 tablet daily EFV: 1 tablet daily **Total**: **2 tablets daily**	50%
3. Tolerability (100%-ADR)	AZT, 3TC, NVP — 9/25 x 100=36% **Tolerability=100-36=64%**	64%	TDF, 3TC, EFV — 11/25 x 100 =44% **Tolerability = 100-44 = 56%**	56%
4. Food Interaction	AZT: 100% (NSFI) 3TC: 100% (NSFI) NVP: 100% (NSFI) **Mean: 100%**	100%	TDF 20% (FIBISE) 3TC: 100% (NSFI) EFV:0% (F1BISE) **Mean 40%**	40%

Adapted in tabular form from[16,17,18]

NSFI: No Significant Food Interaction, **FIBISE:** Food Increase Bioavailability to Increase Side Effect

Decision Analysis of Therapeutic Options in First line Antiretroviral Regimen

In the first line antiretroviral regimen, the criterion rating for AZT+3TC+NVP were 22.5 (efficacy), 5 (daily pill burden), 12.8 (tolerability), 20 (food interaction) with sum of criterion rating (effectiveness) of 60.3.

Similarly, the criterion rating for TDF+3TC+EFV were 23.1 (efficacy), 5 (daily pill burden), 11.2 (tolerability), 8 (food interaction) with sum of criterion rating (effectiveness) of 47.3 as indicated in Table 2

Table 2: Decision Analysis of Therapeutic Options in the first line Antiretroviral Regimen

	Option I: AZT+3TC+NVP			Option II: TDF+3TC+EFV		
Criteria	**Value X**	**Assigned Weight Y**	**Criterion Rating (x*Y)**	**Value X**	**Assigned Weight Y**	**Criterion Rating (X*Y)**
Efficacy	75	0.3	22.5	77	0.3	23.1
Daily Pill Burden	50	0.1	5	50	0.1	5
Tolerability	64	0.2	12.8	56	0.2	11.2
Food Interaction	100	0.2	20	40	0.2	8
Sum of criterion rating (Effectiveness)			60.3			47.3

Source: Adapted[13]

Effectiveness Rating of Therapeutic Options in second line Antiretroviral Regimen

The values for effectiveness rating of antiretroviral drugs criteria for effectiveness from review of literature[16,17,18] were73.3% (efficacy), 16.7% (daily pill burden), 48%(tolerability), 100%(food interaction) for AZT+3TC+LPV/r and 75.3% (efficacy), 20%(daily pill burden), 48%(tolerability), 73.3%(food interaction) for TDF+3TC+LPV/r in the second line antiretroviral regimen. The details are as indicated in Table 3.

Table 3: Effectiveness Rating of Therapeutic Options in second line Antiretroviral Regimen

Criterion	Option I: AZT+3TC+LPV/r	Value	Option II: TDF+3TC+LPV/r	Value
1. Efficacy	AZT: 75% 3TC: 80% LPV/r: 35% **Mean: 73:3%**	73.3%	TDF: 81% 3TC: 80% LPV/r: 65% **Mean: 75.3%**	75.3%
2. Daily Pill Burden	AZT+3TC combination: 2 tablets/day LPV/r combination: 4 tablets/day **Total: 6 tablets/day= 100/6 = 16.7%**	16.7%	TDF+3TC combination: 1 tablet/day LPV/r combination:4 tablets/day **Total: 5 tablets perday=100/5=20%**	20%
3. Tolerability (100%-ADR)	AZT, 3TC, LPV/r } 13/25 x 100 = 52% **Tolerability = 100-52% = 48%**	48%	TDF, 3TC, LPV/r } 13/25 x 100 = 52% **Tolerability = 100-52% = 48%**	48%
4. Food Interaction	AZT: 100% NSFI 3TC: 100% NSFI LPV/r: 100% NSFI **Mean: 100%**	100%	TDF: 20% FIBISE 3TC: 100% NSFI LPV/r: 100% NSFI **Mean: 73.3%**	73.3%

Source: Adapted in tabular form from[16,17,18]

NSFI: No Significant Food Interaction **FIBISE:** Food Increase Bioavailability to Increase Side Effect

Decision Analysis of Therapeutic Options in the second line Antiretroviral Regimen

In the second line antiretroviral regimen, the criterion rating for AZT+3TC+LPV/r were 22.0(efficacy), 1.67 (daily pill burden), 20 (tolerability), 20 (food interaction) with sum of criterion rating (effectiveness) of 53.3 [13].

Similarly, the criterion rating for TDF+3TC+LPV/r were 22.6 (efficacy), 2 (daily pill burden), 9.6 (tolerability), 14.7 (food interaction) with sum of criterion rating (effectiveness) of 48.9 [13]. The details are as shown in Table 4.

Table 4: **Decision Analysis of Therapeutic Options in 2nd line Antiretroviral Regimen**

Criteria	Value A	Assigned Weight B	Criterion Rating a*B	Value A	Assigned Weight B Criterion Rating	A*B
Efficacy	73.3	0.3	22.0	75.3	0.3	22.6
Daily Pill Burden	16.7	0.1	1.67	20	0.1	2.0
Tolerability	48	0.2	9.6	48	0.2	9.6
Food Interaction	100	0.2	20	73.3	0.2	14.7
Sum of Criterion Rating			53.3			48.9

Source: Adapted[13]

Cost-Effectiveness Analysis (CEA) of AZT+3TC+NVP versus TDF+3TC+EFV and AZT+3TC+LPV/r versus TDF+3TC+LPV/r in management of HIV/AIDS Patients on first and second line Regimen respectively

There was statistically significant difference in the effectiveness of AZT+3TC+NVP and TDF+3TC+EFV*.AZT+3TC+NVP costs N70 ($0.23)per unit of effectiveness while TDF+3TC+EFV costs N104 ($0.35) per unit of effectiveness.Therefore, AZT+3TC+NVP appeared to be more cost-effective in the management of HIV/AIDS patients as first line regimen.There was no statistically significant difference in the effectiveness of AZT+3TC+LPV/r and TDF+3TC+LPV/r**.

AZT+3TC+LPV/r cost less N291 ($0.97) per unit of effectiveness relative to TDF+3TC+LPV/r which cost N311 ($1.03) per unit of effectiveness. Therefore, AZT+3TC+LPV/r appeared to be more cost effective than TDF+3TC+LPV/r as second line regimen in the management of HIV/AIDS. See Table 5 for details.

Table 5: Cost-Effectiveness Analysis (CEA) of AZT+3TC+NVP versus TDF+3TC+EFV and AZT+3TC+LPV/r versus TDF+3TC+LPV/r in management of HIV/AIDS Patients on First and Second line Regimen respectively

Regimen	Treatment Option	Total Cost (c) in Naira ($)	Effectiveness	CEA(C/E)
1st Line	**Option 1** AZT+3TC+NVP I b.d x 3/12	5,360($ 17.9)	*60.3	N89 ($0.3) per unit of effectiveness
	Option II TDF+3TC+EFV I o.dx3/12	6,360($21.2)	*47.3	N134 ($0.45)per unit of effectiveness
2nd Line	**Option 1** AZT+3TC I b.d x 3/12 LPV/r II b.d x 3/12 I b.d x 3/12	20, 205($67.4)	**53.3	N379 ($1.26) per unit of effectiveness
	Option II TDF+3TC I o.d x 3/12 LPV II o.dx 3/12	19,698($65.7)	**48.9	N403 ($1.34) per unit of effectiveness

*(χ=4.54; P=0.03; df=1), **(χ=0.01; P=0.369; df=1)

Sensitivity Analysis for Cost Effective Analysis of AZT+3TC+NVP versus TDF+3TC+EFV and AZT+3TC+LPV/r versus TDF+3TC+LPV/r in management of HIV/AIDS Patients on first and second line regimen respectively

Sensitivity Analysis was performed to test whether the decision changes when specific variables (e.g cost, effectiveness) was altered within reasonable range in favour of less cost effective option, TDF+3TC+EFV in first line regimen and TDF+3TC+LPV/r in the second line regimen.

Sensitivity Analysis indicated that the decision remain valid, confirming AZT+3TC+NVP to be more cost effective as first line regimen. It howeverindicated that AZT+3TC+LPV/r was not necessarily more cost effective than TDF+3TC+LPV/r as second line regimen in range of alteration of the respective variables. (Table 6).

Table 6: Sensitivity Analysis for Cost Effective Analysis of AZT+3TC+NVP versus TDF+3TC+EFV and AZT+3TC+LPV/r versus TDF+3TC+LPV/r in the management of HIV/AIDS Patients on 1st and 2ndline regimen respectively

Regimen	Alteration in Variable	CEA
1st line regimen	I. Increasing the cost of AZT+3TC+NVP by 10%	N98 ($0.32)per unit of effectiveness
	ii. Decreasing the effectiveness of AZT+3TC+NVP by 10%	N99 ($0.33)per unit of effectiveness
	iii. Decreasing the cost of TDF+3TC+EFV by 10%	N121 ($0.40)per unit of effectiveness
	iv. Increasing the effectiveness of TDF+3TC+EFV by 10%	N122($0.41)per unit of effectiveness
2nd line regime	I. Increasing the cost of AZT+3TC+LPV/r by 10%	N417 ($1.39) per unit of effectiveness
	ii. Decreasing the effectiveness of AZT+3TC+LPV/r by 10%	N421($1.40)per unit of effectiveness
	iii. Decreasing the cost of TDF+3TC+LPV/r by 10%	N362($1.21)per unit of effectiveness
	iv. Increasing the effectiveness of TDF+3TC+LPV/r by 10%	N366($1.22)per unit of effectiveness

DISCUSSION

Antiretroviral drugs utilization in this study showed consistent use of combination of three antiretroviral drugs. This finding support previous report that treatment of HIV infection with a combination of three antiretroviral drugs is a cost-effective use of resources. [19]

There was statistically significant difference in the effectiveness (outcome) of AZT+3TC+NVP and TDF+3TC+EFV, with AZT+3TC+NVP being more effective as first line antiretroviral regimen. This finding is consistent with their documented tolerability and food interaction indices applied as criteria of their effectiveness rating. These indices were higher in value for AZT+3TC+NVP.[18,20]

Cost Effectiveness Analysis revealed that AZT+3TC+NVP which was more frequently prescribed in the present study, was more cost-effective than TDF+3TC+EFV as first line regimen. This contradicts previous researchers who reported that less cost effective antimicrobials in the treatment of tuberculosis were widely used in health institutions even when more cost effective options were available.[21]The result of this study is significant because it suggest that amidst irrational antimicrobial prescription as reported by earlier workers, anti-retroviral drugs were being prescribed rationally. This may be responsible for the anti-retroviral treatment effectiveness story[22], that people living with HIV are living longer and AIDS- related deaths decreased from 2.2 million in 2010 to 1.8 million in 2015 while about 2.5 million deaths were averted since 2000 in low- and middle-income countries due to increased access and rational HIV treatment. [22]

The finding in the present study is significant as it provides evidence-based information that could be used to sustain and even enhance prescription practice by using the information for educational intervention at prescribers' and managerial level. This would motivate prescribers' more in rational prescribing. The resultant effect will be cost savings and deaths averted by more cost effective antiretroviral therapy. The benefit of consistently following evidence based guideline is cost-effective prescribing.

The better cost effectiveness ratio of AZT+3TC+NVP over TDF+3TC+EFV could probably be due to lower cost and higher effectiveness of AZT+3TC+NVP derived from efficacy, daily pill burden, , tolerability and food interaction indices employed as criteria for effectiveness rating. The finding from the present study is in agreement with the result of a similar generalized cost effectiveness analysis for antiretroviral regimen in a low income countries where discounted cost per quality adjusted life years ofUS$641 using AZT+3TC+NVP and US$ 618 using d4+3TC+NVP were

reported.[23] However, AZT+3TC+NVP showed cost effectiveness of 10.49 quality adjusted years compared with TDF+3TC+EFV, having 11.27 quality adjusted years in United States, a more developed country.[24] Higher rate of resistant cases may be responsible for the observation in the US study.

There was no statistically significant difference in the effectiveness of AZT+3TC+LVP/r and TDF+3TC+LVP/r as second line antiretroviral regimen. AZT+3TC+LVP/r which was more frequently prescribed, appeared to, but not necessarily more cost effective than TDF+3TC+LVP/r as second line antiretroviral regimen in the present study.

Better cost-effectiveness in the use of LPV/r as second line antiretroviral regimen than Nefilriavir (NFV) based on efficacy and resistance had earlier been reported. [24]

The results of the present study support the fact that cost effectiveness analysis could help to make decisions about whether new drugs should be included in a drug formulary list where decisions are made as previously reported. [25] These decisions are made based on the principle that if a drug is not better than a comparable product, it should not cost more, if it is superior to existing therapies but more expensive (a common situation) and funds are available, any extra expenditure should represent "value for money.[26]

The present finding is significant because it has given a guide to institutional treatment and formulary system development for anti-retroviral therapy based on cost effectiveness.

It has been reported that the use of valid economic evaluation methods to measure the value and impact of new services can increase acceptance of such programs by the medical profession, donor agencies and consumers.[4,5,6] Cost Effective therapy of HIV/AIDS will not only ensure rational drug use but also reduce incidence of therapeutic failure by enhancing economic, clinical and humanistic outcome of therapy. Complications due to this disease would be reduced and improvement of patients' quality of life would be achieved. People living with HIV/AIDS's life would also be prolonged. Cost Effectiveness, a form of pharmaco-economic tools appear effective when applied properly in therapeutic decision making.[4,5,6] The various outcomes of therapy namely: economic, clinical and humanistic (psycho-social) outcomes are considered.[26] Pharmacoeconomic principles should be adopted in our National Health Policy, hence its application at all levels of our healthcare delivery system in taking therapeutic and other healthcare intervention decisions.

The result of this study is evidence-based, and be can be used to enhance prescription practice through educational intervention at prescribers and managerial levels. These two should be used to enhance and/or support regulatory intervention. National/Institutional Treatment Guideline for antiretroviral therapy and Hospital Drug Formulary based on cost-effectiveness should be developed using this and/or similar research methodology.

One of the limitations of pharmacoeconomic methodology is that the criterion value and assigned weight which determines the criterion rating is somewhat arbitrary hence, fairly subjective. However, each treatment option was treated identically with respect to the assigned weight to limit the subjectivity and the value to be given to each characteristic (criterion) is determined by the decision maker who will use the result of analysis in taking decision.[13]

CONCLUSION

AZT+3TC+NVP which was more frequently prescribed was more cost effective as first line therapy of cART compared to TDF+3TC+EFV.

AZT+3TC+LVP/r which was more frequently prescribed, appeared to be more cost-effective than TDF+3TC+LVP/r in second line cART.

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REFERENCES

1. Kennedy DA, Hart J, Seely D(2009).Cost Effectiveness of Natural Health Products: A Systematic Review of Randomized Clinical Trials Evid Based Complement Alternat Med. 6(3): 297–304.
2. Kesselheim AS, Avorn J, Sarpatwari A (2006).The High Cost of Prescription Drugs in the United States Origins and Prospects for Reform *JAMA*. 316(8):858-871.
3. Gauvreau CL, Ungar WJ, Köhler JC, Zlotkin S (2012). The Use of Cost-Effectiveness Analysis for Pediatric Immunization in Developing Countries. Milbank Q 90(4): 762–790.
4. Ray M (1979). Pharmaco-economics In: Remington, A. Text Book of PharmaceuticalScience and Practice of Pharmacy

19th edition. Mack publishing Company, Easton Pennsylvania, p1931-1933.

5. Mc Ghan W (1993). Pharmaco-economics In: Remington Text Book of PharmaceuticalScience and Practice of Pharmcy. 19thedition. *Mack Publishing Company*, Easton Pennsylvania p1929-1930
6. Bootman JL, Townsend RJ, Mc Ghan WF (1996). Pharmcoeconomics in: A systematic review of randomized clinical trial in Canada In: Canadian Self CareIndustry Profile of Non-Prescription Drug Manufacturers Association of Canada, Canada p 1-208.
7. Townsend RH(1987). Post marketing Drug Research and Development. *Drug Intelligence and Clinical Pharmacy* 21: 134-136.
8. World Health Organization (1996). Task force on health economies and health sector reform report (/HE/HSR/75) p 1-56.
9. WHO (2009): HIV/ AIDS implementation meeting presentation by Kevin M. De Cock,Director of HIV/AIDS Department, Question and Answer Archives http www.who.Int / features/com.Revision of WHO ART guideline
10. World Health Organization (2009). Measuring medicines prices, availability, and affordabilityand price components. WHO/PSM/PAR/2008.3,2nd edition, *World HealthOrganization*, Gevneva, 1-48.
11. Ganguli A, Clewell J, Shillington AC (2016). The impact of patient support programs on adherence, clinical, humanistic, and economic patient outcomes: a targeted systematic review. *Patient Prefer Adherence* 10: 711–725.
12. Araoye MO(2004). Research methodology with statistics for health and social sciences. 2nd ed.; Ilorin: *Nathadex* p115-121
13. Cano SB, Fujita NK (1998). Formulary Evaluation of Third Generation Cephalosporins using decision analysis. *American Journal of Hospital Pharmacy* 45: 566-569.
14. Jolicoeur LM, Jones-Grizzle AJ, Boyer JG (2002). Guidelines for performing a pharmacy-economic analysis. *American Journal of Hospital Pharmacy* 49:1741-1747.
15. Murray CJI (2000).Development of World Health Organization Guidelines on Generalized Cost Effectiveness Analysis. *Health Economics* 9 (3): 235-251.
16. Gay CL, Mayo AJ, Mfalila CK, Chu H, Barry AC(2011). Efficacy of NNRTI-based antiretroviral therapy initiated during acute HIV infection. *AIDS* 24; 25(7):941-949.
17. Safadi R, Xie Q, Chen Y, Yin KY, Wei L, Hwang SG (2011). Efficacy of switching to telbivudine in chronic hepatitis B patients treated previously with lamivudine. *Liver Int* 31(5):667-75.
18. Sierra-Madero J1, Villasis-Keever A, Méndez P, Mosqueda-Gómez JL, Torres-Escobar I, Gutiérrez-Escolano F (2010). Prospective, randomized, open label trial of Efavirenz vs Lopinavir/Ritonavir in HIV+ treatment-naive subjects with CD4+<200 cell/mm3 in Mexico. *J Acquir Immune Defic Syndr* 53(5):582-8.
19. Yilmaz A, Price R.W, Gisslen M (2012). Antiretroviral drug treatment of CNS HIV-1 infection. *J Antimicrob Chemother* 67(2):299-311.
20. Park H, Park JY, Kim SU, Kim DU, Han K., Chon CY *et al* (2013). Efficacy of switching to telbivudine plus adefovir in suboptimal responders to lamivudine plus adefovir. *World J Gastroenterol* 19(43): 7671–7679.
21. Suleiman IA, Tayo F (2001). Pharmaco-economic Evaluation of Streptomycin Versus Ethambutol in the Treatment of Tuberculosis in Lagos University Teaching Hospital. *Nigeria Quarterly Journal of Hospital Medicine* 11 (1-4): 3-7.
22. UNAIDS. Report on Global AIDS epidemic. Western and Central Africa overveiw. *World Health Organization*, Geneva. 2017; p76-978.
23. Estill J, Salazar-Vizcaya L, Blaser N, Egger M, Keiser O (2017). The Cost-Effectiveness of Monitoring Strategies for Antiretroviral Therapy of HIV Infected Patients in Resource-Limited Settings: Software Tool. PLoS ONE 2015; 10(3) availabel online at (last assessed in September 23rd 2017) https://doi.org/10.1371/journal.pone.0119299
24. Simpson K.N, Jones W.J, Rajagopalan R, Dietz B (2007). Cost Effectiveness of Lopinavir/Ritonavir Compared with Atazanavir plus Ritonavir in Antiretroviral-Experienced Patients in the US. *Clin Drug Invest* 27(7):443-452.