



The Extent, Quality and Features of HIV Costs Evaluation Publications in Nigeria: A Systematic Review

Giwa H. B.^{*1,2}, Davari .M², Nabizade.A², Giwa .A¹, Jamiu M.O.¹, Njinga N.S¹, Abdul.A^{1,3}, Eniayewu O.I¹, Giwa F.A.S⁴

1 Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, University of Ilorin, P.M.B. 1515, Ilorin, Kwara State, Nigeria

2 Department of Pharmaco-economics and Pharmaceutical administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

3 Department of Computer Science, Faculty of Information and Communication Technology, Kwara State University, Malete, Kwara State, Nigeria

4 Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

*Corresponding author: hbfgiwa@yahoo.com

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Citation Giwa HB, Davari M, Nabizade A, Giwa A, Jamiu MO, Njinga NS, et al. The extent, quality and features of HIV cost evaluation publications in Nigeria: a systematic review. Journal of Pharmacoconomics and Pharmaceutical Management. 2025;11(3):36-48.

Running Title HIV Costs Evaluation Publications in Nigeria: A Systematic Review

Article Type Review Article

Highlights

- This systematic review assessed the scope, methodological quality, and features of published HIV cost evaluation studies in Nigeria.
- Of 11 included studies, the mean quality score was 10.56; five were fair and six good, with quality not significantly related to country, publication type, or funding source.
- None assessed indirect medical costs, and all were published in foreign journals, highlighting the need for indigenous research capacity, local/African journal dissemination, and research-policy partnerships.



Article info**Received:**

15.10.2025

Accepted:

02.12.2025

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ABSTRACT

Objective: Nigeria bears a high prevalence of HIV, and donor funding for HIV programs has been known to decline in previous years. This makes the judicious use of healthcare resources paramount. Cost evaluation is important for sustainable HIV financing and policy decisions, however, the scope and quality of HIV cost evaluation studies are unknown. This systematic review investigates the scope, methodological quality, and features of published HIV cost evaluation studies, with the intent of highlighting knowledge gaps and strengthening economic evidence base for HIV program planning.

Method and Results: A search for some databases was conducted using relevant search strategies. Eleven HIV Cost evaluation studies published in 9 journals outside Nigeria were identified. Based on a 14 point score, the mean score of the studies was found to be 10.56. Five studies were rated fair and six rated good. The quality of the study was not significantly related to the country, type of publication and funding source ($p>0.05$). There was no significant correlation between the quality of studies and number of authors, year of publication, cost estimates and sample size ($p>0.05$). The studies captured HIV related cost outcomes which included direct medical costs, willingness to pay, catastrophic expenditures, and the cost effects of decentralization. None of the studies assessed indirect medical cost.

Conclusion: HIV Cost evaluation studies were found to be limited in number though of good quality. All published in foreign journals. This emphasizes the need for building indigenous research expertise, promoting dissemination in local or African journals and encouraging research policy partnerships.

Keywords: Assessment, Cost Evaluation, HIV/AIDS, Nigeria, Systematic Review

Introduction

Pharmaco economics has been defined as the description and analysis of costs of drug therapy to health care systems and society. It identifies, measures and compares the costs/consequences of pharmaceutical products and services[1]. Pharmaco-economics can be used to compare the total costs outcomes of treatment options [1]. Figure1 shows a pharmaco-economic equation in which the left side of the equation represents inputs or cost used to obtain a pharmaceutical product or service. The right side of the equation represents outcomes associated with this option. The center of the equation is the drug product or service being assessed, symbolized by RX. If only the left-hand side of the equation is measured without regard for outcomes, it is a

cost analysis / evaluation (or a Partial pharmaco economics analysis). However, if only the right-hand side of the equation is measured without regard to costs, it is a clinical or outcome study (not an economic analysis) [1]. In general terms, Cost evaluation is the process of determining how resources are used [1]. Cost evaluations provide important insight into the economic burden of disease and can be useful for understanding the resources incurred by health systems, other payers, and patients. Such understanding will aid in the planning of quality care and provide insight into system performance [2]. Summarily data obtained from Cost evaluation studies are important for decision making



Figure 1 Figure 1 Pharmaco Economic Equation [1]

HIV / AIDS is not only the most serious epidemic in modern times but also the greatest public health challenge in history. The concerted effort of scientists was rewarded with success as they were able to turn the epidemic from a fatal to a chronically manageable one. As a result, the life expectancy of patients improved except for patients that start therapy with low CD4 cell counts[3].

High financial commitment in industrialized countries together with rapid uptake and retention of patients in therapy has led to the so-called "Lazarus syndrome" [4]. The syndrome is characterized by the restoration of the health of many terminally ill people in these countries. The challenge here is that the majority of people living with HIV/AIDS (PLWHIV) reside in developing countries/ resource-limited settings where the huge expenditure required for management of the disease is not affordable [4]. This problem of affordability is further aggravated by an increase in the life expectancy of these patients which increases the cost of management of the disease as these patients are more affected by comorbid conditions associated with old age [5].

Africa is experiencing a double burden of disease. This is defined by the growing prevalence of chronic non-communicable diseases (NCD) and the fight against infectious diseases [6].

Nigeria has been faced with many problems in recent years; Apart from the rise in burden of HIV / AIDS, malaria and tuberculosis [29], health care costs have soared and medical treatment is costly and unaffordable for most people [1][7]. Universal health coverage is very low [30]. Funding of HIV / AIDS is largely borne by international donors in Nigeria [8]. The donor community is increasingly looking for ways of moving responsibility for support to developing countries, Nigeria inclusive [8]. Since the commencement of antiretroviral therapy use, there has been a large gap between available funding and the funding needed to meet global HIV / AIDS targets. This is why sustained and coordinated efforts across international and domestic development partners are needed to end AIDS by 2030 [9]. Evidence of increasing funding requirement is shown in the fact that total HIV / AIDS spending in Lower Middle Income Countries (LMICs) increased from \$4.0 billion to \$19 billion between 2000 to 2016.

Most of these potential resources are concentrated in 10 middle-income countries, including Nigeria. Increased funding into future years also anticipated as a result of change in antiretroviral therapy initiation strategies[10].

Having emphasized the importance of Cost evaluation studies to decision making, it will be significant to evaluate the quantity, features, quality and of Cost evaluation studies in the field of HIV and ascertain if these studies are of good quality as good quality data would serve as a reliable guide to effective and efficient use of healthcare resources by decision makers. However It has been reported that the conduct of health economic (including pharmaco-economic) research in Nigeria was limited and about two-thirds of published articles were of sub-optimal quality[7]. Another study reported that the use of health economic (including pharmaco-economic) evaluation research in Zimbabwe was low and 31 % of the studies were of poor quality [11]. China-Based pharmaco-economic studies written in English were found to be limited in number, but on average, were of good quality [12]. This study aims to determine the quantity, features, and quality of Cost evaluation (Partial Pharmaco-economic) studies, regarding HIV/AIDS for Nigeria

Methods

The preferred reporting items for systematic reviews and Meta-Analysis (PRISMA) statement was used to conduct this systematic review[13].

Search Strategy

The PUBMED, Econlit, Embase and Health Technology assessment (HTA) data bases were searched for all relevant published articles. The duration of 10 years before now was considered.

The subject headings (MESH) and text words were used to identify related articles. These strategy is stated thus :(cost*) or economic*) or valu*) or pharmac*) or impact) or burden) or drug expenditure*) or willingness) or employment) or resource*) or use*) or utilization) and hiv*) or aids) or antiretroviral therapy) and Nigeria and "last 10 years"[PDATat] and humans[mesh].

The literature searches were imported into EndNote (version X8) to integrate collected references from different databases, eliminate duplication and promote the review process.

Inclusion criteria

This work is structured to identify and include all original articles published in Nigeria over the past 10 years (for recent data) that included Cost evaluations of HIV / AIDS. The original articles of interest were those that sourced information from databases and patient questionnaires. All included studies were Partial Pharmacoeconomic evaluations such as cost of illness analysis, willingness to pay, catastrophic expenditure, and cost effect of decentralization were all included in this study.

Exclusion Criteria

We excluded studies that were not Cost evaluation studies, not conducted in humans, not including HIV/AIDS treatments, not for Nigeria and not performed within the last 10 years.

Data extraction

All retrieved articles in the initial search were read independently by two reviewers (HB and AZ). First, titles and abstracts were screened, based on the eligibility criteria. Then full-text screening was subsequently carried out, which was also based on eligibility criteria. Any disagreements were discussed and resolved by consensus or by a third independent reviewer (MD) if necessary. The results were then recorded on tables. Table A. 1 Included articles and their journal of publication Tables A. 2 and A. 3 illustrate features of the studies (distinctive attributes) while table A.4 shows cost estimates (product of cost estimation process) across the studies respectively. The mean cost from each study was adjusted using the Medical Consumer Price Index (MCPI) inflation rates found at the Bureau of Labor Statistics' website and converted to the 2019 value. This was based on methodology derived from [14]. Medical Consumer Price Index (MCPI) inflation rates for this study was 5% with a factor of $(1 + MCPI)^t$. Small letter (t) indicated the number of years into the future.

Data Extraction and Quality assessment

A data collection form was developed based on the Drummond checklist for economic evaluations and was adapted for assessing the quality of the included studies (Appendix 1) [14]. The Drummond checklist is a well-established critical appraisal tool for evaluating the methodological quality of economic evaluations. It comprises 10 key questions that

guide the assessment of full pharmacoeconomic evaluations. For the purpose of this study, the checklist was adapted by selecting seven questions considered most relevant to the quality assessment of cost evaluation studies. This instrument has been utilized in previous published studies [7,11,15], and evidence indicates that the Drummond checklist is the most widely used tool for health economic evaluations between 2010 and 2018 [16], owing to its demonstrated reliability and validity.

All the questions were considered to have equal weights. The assessment was executed independently by two reviewers (HB and AZ), and discrepancies resolved by third party MD. The grading was done using a maximum grade of two points for each question, as this makes the award of points easier. Thus, the full mark for each study was 14. Studies with scores below 7 were rated as poor, 7- 10 score were considered as a fair, and 10–14 scores were considered very good quality.

Other Data Collection Tools

Another data collection form was designed to document information such as general study characteristics, including the country in which the journal is based, type of journal (medical or non-medical), funding source, and country coverage, etc. There was also another section for documenting cost-evaluation information, such as the type of cost estimate, value of the cost estimate, sample size for each study, etc. Subjective scores were also included in this form.

Data analysis

Each of the reviewers was labeled as either reviewer 1 or 2; the total score for each study was then assessed for correlation using the Pearson's moment test. The average of these two scores was then found and used as the quality score where ever quality score was required.

To determine the difference between the mean of categorical groups such as country of origin of journal, independent t-tests or ANOVA was used, Pearson's correlation coefficients were used to determine the relationship between the mean scores and the number of authors, year of publication and sample size. Data analysis was done using the Statistical Package for the Social Sciences, version 14.0 (SPSS Inc., Chicago, IL, USA). An alpha level of 5% was used for statistical significance (p 0.05).

Results and Discussion

The results consisted of 3 major sections; first the results of the search, second statement of quantity and features of the studies, and third statement of the technical quality of the studies.

Search results

The initial search identified 1461 citations through PUBMED, Econlit, Embase, Health technology assessment (HTA) databases; of these 161 of which were duplicates. Following the removal of duplicates there were a total of 1300 references, which went through title and abstract screening of which 1100 were removed leaving a total of 200 studies. After full-text screening 11 potentially eligible studies were retrieved. The flow chart of the literature search is shown in Figure 2.

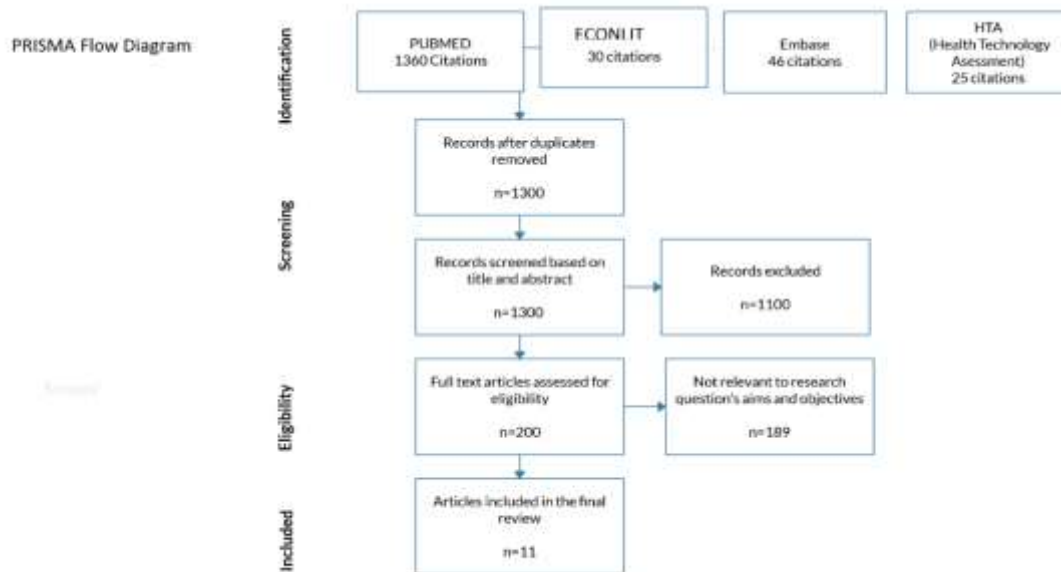


Figure 2 Prisma-Flow-Diagram300 [1]

Quantity and features of the studies.

All selected studies (eleven in number) were published between 2011 and 2018 and outside Nigeria in four different countries. There was no published study in 2014; but 2016 recorded the highest number of published studies, a total of three studies, and then a decline of the number of published studies in 2018 with only two published studies. Three (27%) of the studies were published in United States-based journals, six (54 %) in the United Kingdom-based journals, and one in Switzerland and Ireland-based

journals each (Table 1). Seven (63%) of the articles were published in medical journals and four (37%) in non-medical based journals. The policy-related (non-medical) journals involved included Health Expectations, Health Policy, and Health Policy and Planning journals. A public health journal was also involved which was the Global Public Health journal. Regarding the authors, 53% were resident in Nigeria while the remaining 46% resided outside Nigeria, with 82% of them having medical affiliations

Table 1 Included articles and their journal of publication

Author	Journal	Country of Publication
[8]	J Acquired Immune DeficSyndr	United States
[17]	PLoS One	United states
[18]	Aids	United Kingdom
[19]	PLoS One	United Kingdom
[20]	PLoS One	United states
[21]	J Int AIDS Soc	Switzerland
[22]	Health Expect	United Kingdom
[23]	Health Policy	Ireland
[24]	Health Policy Plan	United Kingdom
[25]	Glob Public Health	United Kingdom
[26]	AIDS Care	United Kingdom

Some features of the studies

The funding sources of the journals ranged from Non-Governmental Organizations (NGOs) such as GHAIN NIGERIA, PEPFAR, and USAID, for 9 articles (81%); the rest of the authors, 2 articles (19%), did not state their funding sources. Six

(55%) of the studies had the perspective of the national health payers while five (45%) had the perspective of the patients. Ten of the studies utilized primary data with only one using secondary data. Table 2.



Table 2 Some features of the studies

		Number of studies	Percentage%
Country In Which the Journal is Based	United States	3	27
	United Kingdom	6	54
	Other Counties	2	19
Total		11	100%
Type Of journal	Medical	7	63
	NonMedical	4	37
Total		11	100%
Type of Cost Estimate	Annual Average Cost Per Patient	4	37
	Other Costs	7	63
Total		11	100%
Funding Source	Non Profit Organizations	9	81
	Not Stated	2	19
Total		11	100%
Country Coverage	National	6	55
	Multinational	5	45
Total		11	100%
The perspective of study	Health payers	6	55
	Patients	5	45
Total		11	100%

Outcome measure and other features of studies

Of all the eleven published articles, 4 [8][17][18][19] featured average annual cost per patient of ART estimation., catastrophic expenditures were investigated by 2 [20][21] willingness to pay for antiretroviral by 2 [22][23], cost-effect of decentralization by 1 [24], effects of criminalization on the cost of management of ART in countries that criminalize same-sex

sexual practices compared to those that don't criminalize same-sex sexual practices (SSSP) by 1[25] and the last study investigated funding and expenditure of community based organization[26]. The developmental stage of the disease (viral load, CD4 counts and clinical staging) was not indicated by all the studies.(Table3)

Table 3: Other features of studies

Author Reference	Outcome Measure	Computation of Cost	Data Source
[8]	Average annual cost per patient of ART*	Top-down	Databases
[17]	Average annual cost per patient of ART*	Bottom-up	Case notes, patient interviews
[18]	Average annual cost per patient of ART*	Bottom-up	Retrospective record review including accounting records, prescribing logs, equipment inventories, and routine reports; key informant interviews
[19]	Average annual cost per patient of ART*	Bottom-up	Accounting records, prescribing logs, equipment inventories, and routine reports; structured interviews with site personnel
[20]	Catastrophic cost	Bottom-up	Patient interviews
[21]	Catastrophic cost	Bottom-up	Pre-tested interviewer-administered questionnaire
[22]	Willingness to pay	Bottom-up	Pre-tested questionnaire
[23]	Willingness to pay	Bottom-up	Pre-tested questionnaire



Author Reference	Outcome Measure	Computation of Cost	Data Source
[24]	Cost effects of service decentralization	Bottom-up	Facility and patient records
[25]	Other related cost studies	Bottom-up	Publicly available documents
[26]	Other related cost studies	Bottom-up	Facility and patient records

Anti-retroviral therapy ART*

The average annual cost per patient of ART was \$241 or \$294 for facilities located in Nigeria. The main cost drivers being ART, human resources and test kits, willingness to pay for anti retrovirals, regarding outpatients was 16.08 or

\$4.94, unsubsidized cost was catastrophic to households (10-40% higher than household cost) was \$6.355 or \$7.06 for outpatients and decentralization of facilities either increase or decrease cost in some settings and dependent on task shifting employee assignation (Table 4).

Table 4: Cost estimates across studies

Author (Reference)	Sample Size / Setting	Type of Outcome Measure	Mean Cost (USD)	Present Value (2019 USD, 5% Inflation)
[8]	9 facilities	Average annual cost per patient of ART*	HTC*: 7.4ART*: 209	HTC*: 10.46ART*: 294
[17]	80 facilities	Average annual cost per patient of ART*	National: 157Facility-level: 231	National: 164.9Facility-level: 241
[18]	Botswana, Ethiopia, Nigeria, Uganda, Vietnam (43 PEPFAR-supported outpatient clinics)	Average annual cost per patient of ART*	Pre-ART: 202Without ART*: 880With ART*: 298	Pre-ART: 329.03Without ART*: 1,433.42With ART*: 485
[19]	54 clinical sites	Average annual cost per patient of ART*	Pre-ART treatment: 177<6 months: 353 (255–468)>6 months: 222 (161–296)	Pre-ART treatment: 249<6 months: 496>6 months: 312
[20]	3 states	Catastrophic	Outpatient direct medical: 5.49Inpatient direct medical: 122.10	Outpatient direct medical: 6.36Inpatient direct medical: 141.34
[21]	1,200 participants	Catastrophic	Outpatient visits (OPV): 6.1	OPV: 7.06
[22]	Not stated	Willingness to pay	WTP*: 15.32	WTP: 16.08
[23]	Tertiary institutions, Enugu (Nigeria)	Willingness to pay	WTP*: 3.2	WTP: 4.96
[24]	3 states	Cost effects of service decentralization	Cross River: increased cost by 40%Kaduna: reduced cost by 29%	Cross River: increased cost by 40%Kaduna: reduced cost by 29%
[25]	8 countries	Other related cost studies	Countries that criminalize SSSP* spend less money	Countries that criminalize SSSP* spend less money
[26]	3 countries	Other related cost studies	Average CBO* received \$29,800 annually (~\$2,480/month)	Average CBO* received \$39,934 annually (~\$3,323/month)

*ART: Antiretroviral Therapy; HTC: HIV Testing and Counseling; WTP: Willingness to Pay; OPV: Outpatient Visits; CBO: Community-Based Organization; SSSP: Same-Sex Sexual Practices.

Quality of studies

The scores apportioned by the two reviewers was found to have a high Pearson's moment correlation of 0.962 ($p < 0.05$). The mean score of the studies was found to be 10.56 (SD 1.29, range 3.95). Five studies had fair scores (7-10), while the remaining six fell into the category of good scores (10 -14). The quality of the study

was found not to be significantly related to the country of publication ($p > 0.05$) (Table 5). There was not also found any significant correlation between the quality of studies and the number of authors, year of publication, cost estimates achieved and sample size ($p > 0.05$) (Table 6).

Table 4Table 5: Relationship between Categorical groups and mean scores

	Categorical data	Mean of quality* score	Standard Deviation
Country In Which The Journal Is Based $P > 0.05$	United States (3)	10.70	1.48
	United Kingdom (6)	10.60	1.46
	Other Counties (2)	9.93	0.81
Type Of Publication. $P > 0.05$	Medical Journal(7)	10.76	1.37
	Non-Medical Journal (4)	10.21	1.23
Type Of Cost Estimate $P > 0.05$	Annual Average Cost Per Patient(4)	11.64	0.94
	Other Costs (7)	9.95	1.17
Funding Source $P > 0.05$	Non –Profit Organizations(9)	10.54	1.43
	Not Stated(2)	10.68	0.25
Country Coverage $p > 0.05$	National (6)	10.47	1.06
	Multinational (5)	10.68	1.65
The perspective of study $p > 0.05$	Health payers(6)	11.00	1.58
	Patients(5)	10.03	0.68

Table 5Table 6: Relationship between mean quality scores and numerical variable

	Number of Authors	Year of Publication	Sample size	Cost estimates
Pearson Correlation coefficients	- 0.456	0.418	-0.789	0.580
p-value	0.159	0.200	0.21	0.606
N	11	11	4	3

Discussion

Over a 10-year period, only 11 cost evaluation studies on HIV/AIDS were conducted in Nigeria. This limited output is unexpected, given that HIV/AIDS remains one of the highest-burden communicable diseases in both Africa and

Nigeria. This low turnover observed in current study is in accordance with the work of [27][28] which shows that there is a low turnout of Cost evaluation studies for resource-limited settings. It also agrees with [7] which showed that there are few health economic evaluations for

Nigeria. This work also shows similarity to [5], which evaluated the economic impact of HIV/AIDS for 5 European countries and had only 26 studies included for 10 years. This modest number of HIV cost-evaluations for Nigeria shows that more research has to be done in this area.

This challenge of low turnover of studies can be approached by making an attempt to improve number and quality of health economics experts, and this can be done with the government providing scholarships, grants and incentives for the study of health economics and Pharmaco - economics at the masters and PhD level. This specialty could also be made a compulsory part of the curricular in medical-related programs, resource persons to run this programs could be sourced at local and international levels. All these will create an upsurge in research, more so in high-quality research in this area. Enhancing the linkage between these institutions and policymakers will increase the value of Health economic evaluations to policy makers. Policymakers could also facilitate the procurement of research grants. According to [11], the establishment of priority settings, research facilities, and procedures for synthesizing and decentralizing results is also important in improving the quality and also quantity of health economic evaluations. They also emphasized that the improvement of peer review process and adoption of health economic guidelines will serve to increase quality, reduce bias and increase comparability of the studies.

Furthermore, the issue of affordability in low- and middle-income countries (LMICs) like Nigeria, where health spending per capita ranges between \$247 and \$303 underscores the growing need for comprehensive health economic evaluations to inform policy and decision-making [6].

The estimated funding of \$814.7 (\$742.8 to \$923.8) on HIV/AIDS per prevalent case for LMIC [27], exceeds the value (\$241 or \$294) obtained in this study for Nigeria. This is an evidence that the national and international health goals for the disease have not been achieved in Nigeria since achievement of these goals was found to correlate with appropriate funding of the health system [27].

In the current study, HIV/AIDS funding of (\$241 or \$294) apart from indirect and intangible costs not considered by authors of included articles represent 97% - 97.6% of health expenditure *per capita* for Nigeria (\$247- \$303) [32]. Spending 97% of health expenditure *per capita* on HIV/AIDS alone is a great burden considering the fact that Nigeria Health System is already overwhelmed with other communicable and non-communicable diseases [6]. All this goes a long way to demonstrate that improved funding for the Nigerian health system is essential to make healthcare targets achievable. The low willingness to pay underscores the need for public sensitization to enhance willingness to pay and advocacy to Government and Donors for sustainable funding.

Publication of all the articles in foreign journals will not encourage the dissemination of information to Nigerians. The establishment of a more high-quality peer-reviewed journal' could be a remedy to this particular challenge. The fact that more than half of the authors were resident in Nigeria imply more local involvement in these high-quality studies. These resourceful individuals could serve as pool of potential reviewers, lecturers in medical affiliated institutions and link between schools and policymakers.

One of the reasons that could explain the high-quality studies is that most of the authors have medical affiliations and hence more experience in the medical field.

Only very few of the studies (18%) not stating their sources of funding is an indication of transparency of this studies, as opposed to similar studies in this area [11] found 55% not stating and [31] found 33% not stating their sources of funding.

The high quality of all included studies in the current research is a positive development. However, previous workers have found some low quality studies in their inclusions [7, 12]. Publication in foreign journals; this did not give space for comparison between the quality of articles in Nigerian and foreign journals.

Most studies assessed direct cost estimation (average cost per patient Of ART), while others explored economic burden (catastrophic expenditure), behavioral valuation (WTP), and system-level cost impacts (decentralization,

policy effects). Together, they provide a comprehensive view of cost outcomes from patient-level to system-level perspectives in HIV economic evaluations.

Conclusion

Eleven (11) cost evaluation studies, regarding HIV/AIDS were carried out for Nigeria within the past ten years. These studies had high quality and the majority of the authors were resident in Nigeria and with medical affiliations. These authors also showed transparency by stating sources of funding but all articles were published in foreign journals. The studies assessed diverse cost outcomes, including direct treatment costs (average ART cost per patient), economic burden (catastrophic health expenditure), behavioral valuation (willingness to pay), and system-level impacts (cost of decentralization and policy

effects) collectively capturing cost outcomes across patient, household, and health system levels.

Limitations

The quality scores were subjective and could be scored differently by other assessors. The sample size of 11 included studies that were obtained in this review did not allow for regression analysis. Indirect Medical Cost was not obtained in the results of this study as this category of cost was not presented in the various included studies.

Acknowledgement

We would like to thank the Tehran university of medical sciences for funding this work

Conflict of Interest Disclosures

The authors reported no conflicts of interest.

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