COST-EFFECTIVENESS ANALYSIS OF ANTI-DIABETIC THERAPY IN A UNIVERSITY TEACHING HOSPITAL

*Giwa Abdulganiyu[1], Tayo Fola[2]

[1]Department of Clinical Pharmacy and Pharmacy Pharmacy Practice, Faculty of Pharmaceutical Sciences, University of Ilorin, P.M.B 1515, Ilorin, Nigeria.
Tel: +2348036869262
abdulganiyugiwa@yahoo.com

[2] West African Postgraduate College of Pharmacy, Yaba, Lagos, Nigeria,
Tel: +2348033358444
folatayo2001@gmail.com

ABSTRACT

Purpose: To conduct cost-effectiveness analysis of anti-diabetic therapy in a University Teaching Hospital in 2010. **Methods**: A retrospective review of selected case-notes was conducted. World Health Organization Defined Daily Dose Method of evaluating drug use and probability method for potential effectiveness of anti-diabetic therapeutic options from literature analysis was employed in determining cost-effectiveness of each anti-diabetic therapeutic option identified from anti-diabetic drug utilization studies. Sample Size, n=1200. Subjects' case-notes were selected by systematic random sampling (Sampling Interval = 1). **Results**: Glibenclamide (N1.76/unit of effectiveness) which was more cost-effective than chlopropamide (N2.97/unit of effectiveness) in the management of moderate hyperglycemia in non-obese Type II Diabetes Mellitus was more frequently prescribed (81.5%). Glibenclamide + Metformin (N7.63/unit of effectiveness) which was more frequently prescribed (92.5%) was not necessarily more cost-effective than Chlopropamide + Metformin (N9.76/unit of effectiveness) in the management of moderate hyperglycemia in obese Type II Diabetes-Mellitus. Biphasic Isophane Insulin (N12.65/unit of effectiveness) which was more cost-effective than soluble insulin + insulin zinc (N30.37/unit of effectiveness) in the management of serve hyperglycemia in non-obese Type II Diabetes Mellitus was less frequently prescribed (42.3%). Biphasic Isophane Insulin + Metformin (N15.91/unit of effectiveness) which was more cost-effective than soluble insulin + insulin zinc + metformin (N34.45/ unit of effectiveness) in the management of severe hyperglycemia in obese Type II Diabetes Mellitus patients was less frequently prescribed (25%). **Conclusions**: Prescription of lees cost-effective anti-diabetic drugs was rampant in Hospitals.

Keywords: Cost-Effectiveness Analysis, Pharmaco-Economics, Anti-Diabetic Therapy

INTRODUCTION

Health care spending is increasing from government and private stand-point as people make choices to empower themselves [1]. The impact of cost containment is causing administrators and policy makers in pharmacy to examine closely the cost and benefits of proposed and existing programmes. Private employers and public agencies are demanding that health problems be evaluated in terms of clinical and social outcomes related to the cost incurred. 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 programmes by the medical profession, third party payers and consumers [2], [3], [4].

There is increasing competition among health professionals for the limited dollars and resources available within the institutions and communities. Pharmacists will have to compete increasingly with nursing, medical and other groups for adequate reimbursement and payment [5], [6]. Pharmacists must document the cost-benefits of distinct pharmacy services and must develop priorities for those services to compete successfully within various arena.

In spite of aforementioned inherent and obvious predicaments, public expectations from healthcare providers and government are becoming higher on daily basis [7], therefore, there is need for a useful scientific intervention that can facilitate rational decision. In addition, despite wide use of pharmaceuticals, few data exist regarding actual costs and benefits attributable to specific drug therapy. This problem may be attributed to lack of well defined methodologies to evaluate medical interventions.

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 [8], [9].

Pharmaco-Economics has been defined as the description and analysis of cost of drug therapy to health care system and society [8]. 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 [9].

Pharmaco-Economics is based on long-term benefits, whereas physicians are typically forced to seek immediate savings [10]. 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 [9]. Pharmaco-Economics focuses on the costs and benefit of drug therapy and provide a basis for resource allocation and utilization. It is increasingly becoming important for health policy decision-making. It is a young science that will improve in application. Its need is undeniable, especially in developing countries [11].

How can we meet the ever increasing demand for health care, given our limited resources? Health Economics helps to address this issue. It can be seen as a tool to help prioritize health care interventions so that maximum health benefits are provided to the population within the resource constraints that exist [12].

Economic evaluation is a systematic appraisal of costs and benefits of projects or alternative ways of achieving the same outcome, undertaken to determine the economic effectiveness of alternatives [13]. Economic evaluation helps decision makers to determine whether the cost of extra effectiveness provided by a new drug is worthwhile within the budget available. They are not supposed to replace the judgment of health professionals, but should support health professionals and decision makers in making informed decisions [12].

Diabetes Mellitus is a chronic, incurable condition that affects 3% of the Nigerian population [14], [15]. There is evidence that prevalence of non-communicable diseases is increasing, including diabetes mellitus, which if not adequately managed, can result in a wide range of complications that have clinical, social and economic implications, especially due to decreasing age of onset [16]. Impaired glucose tolerance (IGT) of 7.7% rate among Hausa-Fulani in North-Eastern Nigeria who have no history of diabetes mellitus has been reported. It was opined that this would increase incidence of diabetes mellitus, as one in three individual with IGT will develop Type II diabetes mellitus [17]. Although, World Health Organization accorded priority status to diabetes mellitus, 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 both patients and the health sector, and its cost to nations in economic terms, due to the fact that use of anti-diabetic drugs in the management of diabetes mellitus is for the lifetime of the patients from the time of diagnosis [14]. This translates into a substantial cost in drug therapy to the patients and government [16]. Use of pharmaco-economic tool such as cost-effectiveness analysis is not institutionalized in taking therapeutic and other healthcare intervention decisions in Nigeria. The study was aimed at conducting cost-effectiveness analysis of anti-diabetic therapy in a University Teaching Hospital in Nigeria, in 2010. A form of anti-diabetic drugs utilization study and consequently their economic evaluation is needed to promote rational anti-diabetic drugs prescription and improve economic, clinical and humanistic outcome of anti-diabetic therapy.

Cost-effective therapy of diabetes mellitus will not only ensure rational drug use but also reduce patients dropping out of treatment because of cost, thereby reducing incidence of therapeutic failure by enhancing economic, clinical and humanistic outcome of therapy. Complications due to this disease would be reduced and improvement in patients' quality of life would be achieved. Cost-Effectiveness tool appear effective when applied properly in therapeutic decision making. The various outcomes of therapy namely: economic, clinical and humanistic (psycho-social) outcomes are considered [18].

MATERIALS AND METHODS

The study was conducted at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State, Nigeria. The Hospital was chosen because it was the only University Teaching Hospital in North-Eastern Nigeria, serving the six catchment states of North-Eastern Nigeria. Diabetes Mellitus cases were usually referred to UMTH from these catchment states as at the time of conducting this study.

Ethical Approval was obtained from Research and Ethics Committee of UMTH.

Type II diabetes mellitus patients that were registered with and attended the Diabetes clinic of UMTH were the subjects for the study. Their population from inception of UMTH in 1983 to December 2009 was obtained from Medical Record Department and was assumed /used as the estimate of the population size of serviced Type II

diabetes mellitus patients. This was 2,528. Fischer's Formula [19] was applied to determine sample size from this estimate.

The required sample size was 351. However, 1, 200 of estimated population were studied due to availability of resources and to reduce error.

A retrospective review of case-notes of the selected subjects for treatment options identification with diagnosis and average cost for a full course of each identified treatment option involving standard cost-accounting technique was conducted.

The treatment options available for different stages (moderate and severe hyperglycemia in obese and non-obese subjects) of Type II diabetes mellitus was identified from case-notes of the subjects. Pattern of usage of each identified option was determined in an anti-diabetic drugs utilization study.

The study design objective was to determine which of the identified options for different stages of Type II diabetes mellitus were more cost-effective**.** The economic perspective of the subjects was considered since the drug cost was borne by them.

A data collection form was designed (Appendix I) and used to capture data relating to cost component of cost-effectiveness analysis. A standardized effectiveness rating format (Appendix II) and decision analysis table (Appendix III) were designed to document, rate and analyze effectiveness indicators of anti-diabetic drugs generated from literature.

In data collection, patients' code number by hospital number and anti-diabetic drugs prescriptions and other relevant information from case notes were filled into the data collection form (Appendix I). The 1, 200 case-notes were selected by systematic random sampling (using sampling interval of 1).

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

Anti-Diabetic therapy is a life long management but follow up visit to the physician is usually every two months (60 days) for mild hyperglycemia, one month for moderate hyperglycemia and two weeks for severe hyperglycemia [20]. Duration of therapy was therefore respectively set at these periods for each hyperglycemic category identified.

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 UMTH was used.

To avoid bias, average cost of available generic equivalents were considered for all the treatment options and UMTH Pharmacy Price were employed for all.

The effectiveness measure involved theoretical framework by analysis of positive and negative outcome of each treatment option from review of literature as in Appendix II to establish probabilities of the outcomes and applying decision analysis as in Appendix III for effectiveness of chlopropamide and glibenclamide options [21], [22], [23], [24].

Effectiveness of a treatment option (in natural unit) = Sum of all criterion rating, where 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 [21], [22], [23], [24].

Criterion Value was obtained from analysis of positive and negative outcome of different criterion (characteristic) of a treatment option from review of literature in natural unit e.g. percentages [21], [22], [23], [24]. For example, criteria for anti-diabetic drugs effectiveness (outcome) and respective assigned weight include efficacy (0.4), adverse drug reaction 0.2), safety of administration (0.1), frequency of administration (0.1) and bioavailability (0.2) (Appendix III).

Confounding variables were identified and solutions proffered to them right from the study design (Appendix IV).

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 [25].

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.

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

[26], [25].

This was determined and compared for available options in each hyperglycemic category.

Sensitivity Analysis was performed to test whether the decisions change when specific variables (e.g. cost, effectiveness) were altered within reasonable range (10-25%) in favour of less cost-effective option, as in Appendix V for chlopropamide and glibenclamide in the management of moderate hyperglycemia in non- obese Type II diabetes mellitus patients.

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

The limitation of this method is in the fact that 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 (Appendix III).

The value to be given to each characteristic (criterion) is determined by the decision maker who will use the result of analyses in taking decision [21].

RESULTS

Anti-Diabetic Drugs Utilization/Identified Treatment Options for Cost-Effectiveness Analysis

Twenty Four (2%) and 36 (3%) out of 1,200 subjects were managed with diet/lifestyle modification only (for mild hyperglycemia in non-obese Type II DM) and metformin only (for mild hyperglycemia in obese Type II DM) respectively.

One Hundred and Fifty (81.5%) out of 184 non-obese subjects with moderate hyperglycemia were managed with glibenclamide tablet monotherapy while 34 (18.5%) were managed with chlopropamide tablet monotherapy. There was a significant difference in this distribution.

Six Hundred and Thirty Two (92.9%) out of 680 obese Type II diabetes mellitus patients with moderate hyperglycemia were managed with metformin + glibenclamide combination therapy while 48 (7.1%) were managed with metformin + chlopropamide combination therapy.

Ninety (57.7%) out of 156 non-obese Type II diabetes mellitus patients with severe hyperglycemia were managed with soluble insulin + insulin zinc suspension while 66 (42.3%) were managed with biphasic isophane insulin. There was a significant difference in the proportions.

Ninety (75%) out of 120 obese Type II diabetes mellitus patients with severe hyperglycemia were managed with soluble insulin + insulin zinc suspension + metformin while 30 (25%) were managed with biphasic isophane insulin + metformin. There was a significant difference in these proportions. Overall, 900 (75%) of the subjects were managed with oral hypoglycemic agents (Table I).

When effectiveness alone was considered, The criteria rating for effectiveness of chlopropamide was 75.66 while that of glibenclamide was 85. There was no statistically significant difference in the effectiveness of chlopropamide and glibenclamide tablet.

Glibenclamide cost less (N1.76) per unit of effectiveness while chlopropamide cost more (N2.97) per unit of effectiveness. Glibenclamide therefore appeared to be more cost effective than chlopropamide in the management of moderate hyperglycemia in non-obese Type II diabetes mellitus patients (Table 2). Sensitivity Analysis indicates that the decision remain valid, confirming glibenclamide to be more cost effective (Appendix V)).

There was no statistically significant difference in the effectiveness of metformin + chlopropamide (69.33) and metformin + glibenclamide (78.67). However, in cost-effectiveness analysis, Metformin + Glibenclamide cost less (N7.63) per unit of effectiveness while metformin + chlopropamide cost more (N9.74) per unit of effectiveness. Metformin + Glibenclamide therefore appeared to be more cost effective than metformin + chlopropamide in the management of moderate hyperglycemia in obese Type II diabetes mellitus patients (Table 3). Sensitivity Analysis indicates that the decision becomes invalid, showing that metformin + glibenclamide combination was not necessarily more cost effective than metformin + chlopropamide.

There was no statistically significant difference in the effectiveness of soluble insulin + insulin zinc (80.67) and biphasic isophane insulin (83). In cost-effectiveness analysis, Soluble insulin + insulin zinc cost more (N30.37) per unit of effectiveness while biphasic isophane insulin cost less (N12.65) per unit of effectiveness. Biphasic Isophane Insulin therefore appeared to be more cost effective than soluble insulin + insulin zinc in the management of serve hyperglycemia in non-obese Type II diabetes mellitus patients (Table 4). Sensitivity analysis indicates that the decision remain valid, confirming biphasic isophane insulin to be more cost- effective.

There was no statistically significant difference in the effectiveness of soluble insulin + insulin zinc + metformin (77.21) and biphasic isophane insulin + metformin (79.17). .Soluble Insulin + Insulin Zinc + Metformin cost more (N34.45) per unit of effectiveness while biphasic isophane insulin + metformin cost less (N15.91) per unit

of effectiveness. Biphasic Isophane Insulin + Metformin therefore appeared to be more cost effective than soluble insulin + insulin zinc + metformin in the management of serve hyperglycemia in obese Type II diabetes mellitus patients (Table 5). Sensitivity Analysis indicates that the decision remain valid, confirming biphasic isophane insulin + metformin to be more cost effective than soluble insulin + insulin zinc + metformin

DISCUSSION

There was no statistically significant difference in the effectiveness (outcome) of glibenclamide and chlopropamide. This is in line with their documented comparable efficacy, bioavailability, safety and frequency of administration applied as criteria of their effectiveness rating [16], [27]. Cost Effectiveness Analysis, however, revealed that glibenclamide which was more frequently prescribed, was more cost-effective than chlopropamide. This is in agreement with a report that glibenclamide is the drug of choice in the monotherapy of moderate hyperglycemia in non-obese Type II diabetes mellitus [16]. Indeed, glibenclamide has been recommended as the drug of choice in the management of Type II diabetes mellitus and use of chlopropamide discouraged due to its exaggerated hypoglycemic and other side effects when compared with other drugs in the same class [28]. These effects are due to its relatively longer half life (35hours) compared with 24 hours for glibenclamide in the same class. It is also the only drug in its class that exhibit disulfiram like reactions [28].

There was no significant difference in the effectiveness (outcome) measure of metformin + chlopropamide and metformin + Glibenclamide. This result is in agreement with reported fact that there is no evidence to justify benefit of a combination of hypoglycemic agents over another, especially on a long term basis [27]. This result is in line with their documented comparable/apparently equal efficacy, bioavailability, safety and frequency of administration [16], [27]. Cost Effectiveness Analysis which indicated that metformin + glibenclamide combination which was more frequently used was not necessarily more cost-effective than metformin + chlopropamide after sensitivity analysis, is also in support of the same report that there is no evidence to justify benefit of a combination of hypoglycemic agents over another, especially on a long term basis.

Effectiveness Measure (outcome) of soluble insulin + insulin zinc and biphasic isophane insulin revealed no statistically significant difference. This finding agrees with their documented comparable, efficacy, tolerability, bioavailability, safety and frequency of administration [16], [27]. Biphasic isophane insulin which was less frequently prescribed was more cost-effective than soluble insulin + insulin zinc. This result may be probably due to the fact that biphasic isophane insulin is a ready mixed combination of 30% soluble insulin and 70% insulin zinc, long acting with a duration of action of 16-18hours extending to 24 hours in some individuals, eliminates mixing errors and of lower cost than soluble insulin + Insulin zinc combination which may introduce mixing errors [16].

For the same reasons, effectiveness measure (outcome) of soluble insulin + insulin zinc + metformin combination and biphasic isophane insulin + metformin combination in the management of severe hyperglycemia in obese Type II diabetes mellitus revealed that there was no statistically significant difference in their effectiveness.

Biphasic Isophane Insulin + Metformin combination was more cost-effective than soluble insulin + insulin zinc + metformin combination, which is more frequently used at present in the management of severe hyperglycemia in obese Type II diabetes mellitus. There is no justification for this utilization trend from cost effectiveness point of view.

The results of this study support the reported 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. 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” [29].

The present finding is significant because it has given a guide to institutional treatment and formulary system development for anti-diabetic therapy based on cost effectiveness. This study indicates cost-effectiveness of various anti-diabetic therapy options: a guide to rational institutional treatment and formulary system development. Institutional Treatment Guideline for anti-diabetic therapy and Hospital Drug Formulary based on cost-effectiveness could therefore be developed using this and/or similar research methodology. This pharmaco-economic approach is presently lacking in Nigeria public and private Hospitals. The work provides evidence-based information that could be used to change prescription practice- irrational prescription of less cost-effective anti-diabetics over more cost-effective ones, by using the information for educational intervention at prescribers’ and managerial levels. The resultant effect will be cost savings in drug therapy. This is especially important since about 95% of Type II Diabetes Mellitus Patients were managed with anti-diabetic drugs.

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 [2], [3], [4].

CONCLUSION

Glibenclamide which was more frequently prescribed was more cost- effective than chlopropamide in the management of moderate hyperglycemia in non-obese Type II diabetes mellitus patients. Sensitivity analysis in cost-effectiveness analysis indicated that Metformin + Glibenclamide which was more frequently prescribed combination was not necessarily more cost effective than Metformin + Chlopropamide in the management of hyperglycemia in Obese Type II Diabetes Mellitus. Biphasic Isophane Insulin was more cost-effective than soluble insulin + insulin zinc which was more frequently prescribed in the management of severe hyperglycemia in non-obese Type II diabetes mellitus patients. Biphasic Isophane Insulin + Metformin was more cost-effective than Soluble Insulin + Insulin Zinc + Metformin which was more frequently prescribed in the management of severe hyperglycemia in obese Type II diabetes mellitus patients.

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Appendix I: Data Collection Form for Cost Effectiveness Analysis

S/N	Date	Patient's Code Number	Diagnosis and FBS at diagnosis	Weight in kg at diagnosis	Height in Metres at diagnosis	Relevant Diagnostic/Monitoring Test (Latest FBSin mmole/litre)	Relevant Diagnostic/Monitoring Test (Average HbAIc %)	Year of First Diagnosis (Age at Onset in Years)	Concurrent Illness	Prescriptions (Generic/ Branded)	Duration of Present Regimen (Month)	Physician's Remark on Glycemic Control and Regularity on	B.P(mm Hg)	Number of Antidiabetic Drug on Prescription	Number Available	Number Out of Stock			Number of Available ones that are Affordable	Number not Affordable	Defined Daily Dose (DDD)	Cost/DDD	Duration of Therapy	Total Cost of Drugs

Appendix II
Effectiveness Rating of Therapeutic Options for Moderate Hyperglycemia
(FBS 7.8 - 11.1mmole/litre) in Non-Obese Type II Diabetes Mellitus Patients

Criteria	**Option I: Chlopropamide**	**VALUE**	**Option II: Glibenclamide**	**VALUE**
1. Efficacy	Consistent control of blood sugar	80%	Consistent control of blood sugar	80%
2. Adverse Drug Reaction	Hypoglycemia: 100% Disulfiram Like Reactions: 50% Others: 80% Mean = 76.7% Tolerability = 100-76.7 = 23.3%	23.3%	Hypoglycemia: 50% Disulfiram like reactions: 0% Others: 40% Mean = 30% Tolerability = 100-30 = 70%	70%
3. Safety of Administration	Risk of infection: nil Risk of abscess: nil Pain at site of administration: nil	100%	Risk of infection: nil Risk of abscess: nil Pain at site of administration: nil	100%
4. Frequency of Administration	Once Daily with Break Fast (o.d)	100%	Once Daily with Break Fast (o.d)	100%
5. Bioavailability	80% bioavailable after oral administration	80%	80% bioavailable after oral Administration	80%

FBS: Fasting Blood Sugar
Tolerability = 100% - Adverse Drug Reaction.
Assumptions: o.d. = 100%, b.d = 50%, tid = 33.3%, qid = 25%
Sources: adapted in tabular form from: [16], [27].

Appendix III
Decision Analysis of Chlopropamide Only and Glibenclamide Only

	Option I: Chlopropamide			**Option II: Glibenclamide**		
Criteria	**Value (%)**	**Assigned Weight**	**Criteria Rating**	**Value (%)**	**Assigned Weight**	**Criteria Rating**
1. Efficacy	80	0.4	32	80	0.4	32
2. Tolerability	23.3	0.2	4.66	70	0.2	14
3. Safety of Administration	100	0.1	10	100	0.1	10
4. Frequency of Administration	100	0.1	10	100	0.1	10
5. Bioavailability	95	0.2	19	95	0.2	19
Sum of criteria rating (effectiveness)			75.66			85

Sources: adapted from: [21], [22], [23], [24].

Appendix IV
Confounding Variables and Solutions for Cost Effectiveness Analysis

	Confounding Variable	Solution
Cost	Availability of drugs Time of purchase	Mean cost/DDD of available anti-diabetic drugs in UMTH was used. All purchases were within the same year so there was no significant inflationary effect.
Outcome	Other diseases Dose variation of same drugs in different patients Individual variation in response	Probabilities outcome measure was applied using theoretical framework for outcome indicators of the drugs from review of literature. Other diseases do not affect this. Only prescriptions of same drugs in the same dose were analyzed together. The effectiveness (outcome) measure was not prospective, but theoretical framework approach to outcome measure.

Appendix V
Sensitivity Analysis for CEA of Chlopropamide and Glibenclamide in the Management of Moderate Hyperglycemia in Non- Obese Type II Diabetes Mellitus Patients

Alteration in Variable	**CEA**
i. Decreasing the cost of chlopropamide by 25% (N56.25)	$CEA = \frac{168.75}{75.66} = N2.23 / unit\ of\ effectiveness$
ii. Increasing the effectiveness of chlopropamide by 25% (18.91)	$CEA = \frac{225}{94.57} = N2.38 / unit\ of\ effectiveness$
iii. Increasing the cost of glibenclamide by 25% (N37.50)	$CEA = \frac{187.50}{85} = N2.21 / unit\ of\ effectiveness$
iv. Decreasing the effectiveness of glibenclamide by 25% (21.25)	$CEA = \frac{150}{63.75} = N2.35 / unit\ of\ effectiveness$

Table 1: Anti-Diabetic Drugs Utilization/Identified Treatment Options for Cost-Effectiveness Analysis

Condition	**Frequency of Anti-Diabetic Drugs Used**		**Total**	**Chi-Square Analysis**
Mild Hyperglycemia in Non-obese DM	Diet and Lifestyle Modification Only 24 (100%)		24 (100%)	
Mild Hyperglycemia in Obese DM	Metformin Only 36 (100%)		36 (100%)	
Moderate Hyperglycemia in Non-obese DM	Chlopropamide 34 (18.5%)	Glibenclamide 150 (81.5%)	184 (100%)	χ^2 =79.38; df=1; p =0.0000
Moderate Hyperglycemia in Obese DM	Metformin + Chlopropamide 48 (7.1%)	Metformin + Glibenclamide 632 (92.9%)	680 (100%)	χ^2=144.50; df=1; p =0.0000
Severe Hyperglycemia in Non-obese DM	Soluble Insulin + Insulin Zinc + Metformin 90 (57.7%)	Biphasic Isophane Insulin 66 (42.3%)	156 (100%)	χ^2 =4.50; df=1; p =0.034
Severe Hyperglycemia in Obese DM	Soluble Insulin + Insulin Zinc + Metformin 90 (75%)	Biphasic Isophane Insulin+Metformin 30 (25%)	120 (100%)	χ^2 =48.02; df=1; p =0.0000

Table 2: Cost Effectiveness Analysis (CEA) of Chlopropamide and Glibenclamide in the Management of Moderate Hyperglycemia in Non-Obese Type II Diabetes Mellitus Patients

Treatment Option	Total Cost (C) in Naira	* Effectiveness (E)	CEA (C/E)
Option I Chlopropamide Tablet 250 mg o.d x 1/12	225	75.66	N2.97/ Unit of Effectiveness
Option II Glibenclamide Tablet 5 mg o.d x 1/12	150	85	N1.76/Unit of Effectiveness

*(χ^2=2.04; df=1; p =0.153)

Table 3: Cost Effectiveness Analysis (CEA) of Metformin + Chlopropamide and Metformin + Glibenclamide in the Management of Moderate Hyperglycemia in Obese Type II Diabetes Mellitus Patients

Treatment Option	Total Cost (C) in Naira	*Effectiveness (E)	CEA (C/E)
Option I: Metformin Tablet 500 mg tid x 1/12 + Chlopropamide Tablet 250 mg o.d x 1/12	675	69.33	N9.74/unit of effectiveness
Option II: Metformin Tablet 500 mg tid x 1/12 + Glibenclamide Tablet 5 mg o.d x 1/12	600	78.67	N7.63/unit of effectiveness

*(χ^2 =2.10; df=1; p = 0.147).

Table 4: Cost Effectiveness Analysis (CEA) of Soluble Insulin + Insulin Zinc and Biphasic Isophane Insulin in the Management of Severe Hyperglycemia in Non-Obese Type II Diabetes Mellitus

Treatment Option	Total Cost (C) in Naira	*Effectiveness (E)	CEA (C/E)
Option I Soluble Insulin 20 i.u tid x 2/52 + Insulin Zinc 10 i.u o.d x 2/52	2,450.00	80.67	N30.37/unit of effectiveness
Option II Biphasic Isophane Insulin 20 i.u am, 10 i.u pm	1,050	83	N12.65/unit of effectiveness

*(χ^2 =0.03; df=1; p = 0.854)

Table 5: Cost Effectiveness Analysis of Soluble Insulin + Insulin Zinc + Metformin and Biphasic Isophane Insulin + Metformin in the Management of Severe Hyperglycemia in Obese Type II Diabetes Mellitus

Treatment Option	Total Cost (C) in Naira	*Effectivenes (E)	CEA (C/E)
Option I: Soluble Insulin 20 i.u tid x 2/52 + Insulin Zinc 10 i.u o.d x 2/52 + Metformin Tablet 500 mg tid x 2/52	2,660.00	77.21	N34.45/unit of effectiveness
Option II: Biphasic Isophane Insulin 20 i.u am, 10 i.u pm + Metformin Tab 500mg tid x 2/52	1,260	79.17	N15.91/unit of effectiveness

*(χ^2 =0.03; df = 1; p = 0.864)