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Prescription Patterns and Cost Effectiveness of Antiglaucoma Drugs in a Tertiary Hospital in Nigeria

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This study sought to determine the prescribing patterns and designed a treatment guideline for primary open-angle glaucoma (POAG) that is more cost-effective from a third-party payer's perspective than the current practice based on real-world evidence. A retrospective descriptive study on eighty patients on POAG therapy for at least 3 months was carried out. A Stochastic Monte Carlo simulation model based on the outcome and cost was constructed with the aid of Vanguard studio 5.0. The input data were the prices of drugs and the proportion of the patient's intraocular pressure outcome per month. Drug prices were entered as a uniform distribution while the outcome values were fixed. Sensitivity analysis was conducted by varying the input data by ±50%. The frequency of monitoring of patients with intraocular pressure was low (26.76%). The commonly prescribed drugs were the beta-blockers and carbonic anhydrase inhibitors. The cost per patient per annum was estimated at ($490.90) whereas the proposed guideline that results in the improved outcome will cost $50.19. Therefore, cost savings will be obtained by the proposed guideline for POAG per patient per annum.

Key words: Cost-effectiveness, antiglaucoma, treatment guideline

INTRODUCTION

Glaucoma is the second-leading cause of acquired blindness. Therefore, in maintaining patients' quality of life (QoL) it is important to diagnose, treat, and manage the disease so that burden imposed by the disease on society can be reduced. However, glaucoma is syndromically treated thus, the expertise for the treatment and management is essential.

Recently, there has been the introduction of numerous new diagnostic and therapeutic aids in clinical settings, which has made the diagnosis and treatment of glaucoma multi-faceted. However, there still difficulties in selecting appropriate diagnostic and therapeutic measures for the individual patient and ensuring long-term patient management to improve both quality of life (QOL) and quality of vision.

Many countries have documented guidelines for the management of glaucoma. For instance, the Japan Glaucoma Society has a guideline to aid ophthalmologists in medical care for glaucoma patients which include appropriate diagnosis and treatment. The guidelines offer proper standards for current glaucoma treatment. However, it is not intended to impose limitations on physicians in diagnosing various clinical conditions but to serve as a reference for improving the level of care and reducing discrepancies among the various types of treatment provided [1].

The focus has been on glaucoma treatment guidelines that improve the quality of therapy. Moreover, guidelines are also needed to improve communication between patients and caregivers, facilitate the selection of treatment options, provide relevant information to all parties concerned, and facilitate team medical care. Additionally, it is necessary to reduce health care expenses by efficiently utilizing resources from the standpoint of globalization of health care and medical economics.

In the Japanese guidelines, first, the stage of glaucoma, baseline intraocular pressure (IOP) without treatment and other risk factors are established. This is followed by establishing a

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target IOP before the commencement of therapy. If the target IOP is achieved, the treatment is continued whilst iff not and there is the deterioration of the optic nerve and or visual field, the treatment is changed as well as target IOP [1]. On the other hand, in the Canadian guidelines, the therapeutic options for lowering IOP include the use of topical or systemic anti-glaucoma medications, laser trabeculoplasty, surgery to improve outflow facility, and cyclodestructive laser to reduce aqueous production. Patient counselling is also recommended before initiation of therapy. The patient and their caregivers are involved in the therapeutic decision-making process [2].

The monitoring of patients should include documentation of the IOP (method and time measured), patient confirmation of and frequency of medications used, as well as the time of their last medication administration [2]. However, Sleath et al. 2006 [3] and Zhou et al. 2004 [4] asserted that compliance to therapy by the patient is fairly poor. Minimizing the number of medications may improve adherence [5]. There is no clear evidence linking reduced adherence with more rapid visual field (VF) deterioration. However, educating patients about their disease and treatment should ultimately improve patient adherence, and reduce the risk of significant progression [6].

In Nigeria, the standard treatment guidelines (STG), 2008 [7], released by the Federal Ministry of Health, unfortunately, have no recommendation for the treatment and management of glaucoma and the second edition 2016 [8] provided treatment guidelines without classification or categorization of stages in therapeutic management. Hence there is the need to look at the prescribing pattern and also try to establish the cost effectiveness of current medications used as compared to other guidelines.

The objectives of the study were to determine the prescribing pattern for antiglaucoma medication and design a treatment guideline for primary open-angle glaucoma (POAG) that is more cost-effective from the perspective of a third-party payer than the current practice based on real-world evidence.

METHODS

The study was conducted at the University of Benin Teaching Hospital eye clinic. A retrospective descriptive study of glaucoma patients was carried out with the aid of the data collection form. The prices with a 95% confidence limit (CL) of antiglaucoma drugs were estimated from hospital price lists and the five nearby community pharmacies. Eighty randomly selected case notes of glaucoma patients who had been on therapy for at least 3 months that met the criteria and had IOP measurement at the onset to three months were studied. Ethical clearance was sought and obtained with protocol number ADM/E22/A/VOL.VII/830. Data collected were the demographics and diagnosis, IOP measurement and the drugs prescribed per month. Thus only 65 case notes of patients with POAG with complete data for at least one month were used in the model construction.

Data analysis and model construction

Data were entered into Microsoft Excel and analyzed for percentiles, mean and standard deviations. Inferential statistics were done with using GraphPadInStat version 3.0. (Graphpad Software, La Jolla, California, USA). Cost-effectiveness was calculated using the Stochastic Monte model based on the outcome and cost, this was constructed with the aid of Vanguard studio 5.0 (Cary, North Carolina, USA). The input data were 95% CL of the prices of prescribed antiglaucoma drugs and the outcome of the therapy which was entered as the proportion of patients whose IOPs were normal, reduced or either increased or unchanged per month of treatment. The drugs prices were entered as a uniform distribution while the outcome values were fixed. The cost of medications was collected in Nigerian naira (NGN) and converted to United States Dollar (USD) in this report.

The model has three distinct parts the first part is to graphically represent the prescription pattern of antiglaucoma monotherapy for one month and the average cost per patient based on the current care in the study site. The primary purpose of this section was to aid and simplify the design of the proposed guideline.

The second part of the model showed the outcome of the mono and combination therapies for POAG patients who had complete input data for one month based on the current practice in the hospital. The output data was cost effectiveness per month.

The third part of the model was constructed using the outcome of the different antiglaucoma drugs classes and the 95% CL of their prices as model outputs. The principle applied here was that the cheapest but moderately efficacious of the drug was used as first-line treatment while the more expensive class of the drug with higher efficacy was reserved for those who failed to respond to the cheaper class drug after one month of therapy. The implication was that in the presence of limited resources more patients could have their IOP's properly controlled compared to when only the more expensive product was prescribed. This section of the model was for three months where every single patient showed a positive treatment outcome. One thousand (1000) simulations of the cost-effectiveness values were then noted.

Sensitivity analysis

In order to investigate the impact of estimated outcome and prices of the cost-effectiveness of the proposed treatment guideline for POAG, a sensitivity analysis was conducted by varying the input data by ±50%.

Inferential analysis

The statistical significance of the cost-effectiveness of the current practice for one month as compared to that of the proposed guideline for three months using Student's t-test with the aid of GraphPad instant 3.0 (Graphpad Software, La Jolla, California, USA). P values less than 0.05 were interpreted as being significant.

RESULTS

The 80 glaucoma patients from which the study cohort was drawn consisted of 43 males (53.8%) and the rest were females with 65 (81.3%) of patients having POAG. The majority of the glaucoma patients 55 (68.75%) were put different combination drugs at onset and after one month as shown in Table 1. The commonest drugs prescribed were beta-blockers and a combination of beta-blockers with carbonic anhydrase inhibitors. Despite that therapeutic failure was reported with the IOP remaining above normal value (below 21 mmHg) as shown in Table 2.

Similarly, among the 65 POAG patients for whom complete information was available, the same treatment pattern was also used for them. About 33% and 29% of the patients on beta-blockers (BB) and CAI respectively experienced treatment failure since their IOP were either increased or unchanged for the one month for which complete data was available as seen in Table 2. Thirty-five patients were on the same drugs after 1 month. Patients with reduced IOP were 40 while 15 had increased IOP. However, only 33 patients had normal IOP while seven had reduced IOP but it was still greater than 21 mmHg (Table 2). The most prescribed drugs for the POAG patients were beta-blockers and a combination of beta-blockers with carbonic anhydrase inhibitors. Timolol maleate 0.5% is the commonest BB prescribed, while brinzolamide (Azopt®) and Latanoprost 0.005% (Xalatan®) were the frequently prescribed CAI and PG respectively as monotherapy as seen in Table 3.

A model was built from the current practice of prescribing with the prices of prescribed antiglaucoma drugs as input data while the outcome of therapy was entered as the proportion of patients whose IOPs were normal, reduced or either increased or unchanged per month of treatment. The drug prices were entered as a uniform distribution while the outcome values were fixed. (Figure 1). The data was also to model current monotherapy practice and the different combinations based on their prices that gave a cost-effective algorithm that would produce a good therapeutic effect.

There was no significant association between demographics and classes of drugs prescribed (P-value were 0.1983 and 0.7890) as shown in Table 4. Among patients with POAG, there was also no significant association between the classes of drugs prescribed and the demographics of the patients (Table 4).

Table 1: Proportion of glaucoma patients on different classes of drugs at onset and after one-month treatment

Type of therapy	Number of patients at onset [%}	Number of patients on it after 1 month [%]
Monotherapy		
BB-Timolol 0.5%	13 [16.25]	9[11.25]
BB: Betaxolol	3 [3.75]	1 [1.25]
CAI: Azopt®	1 [1.25]	0 [0.00]
CAI: Acetazolamide	0 [0.00]	1 [1.25]
PG: Xalatan®	1[1.25]	0 [0.00]
PARA: Pilocarpine 4%	0 [0.00]	1 [1.25]
Multivitamins	1 [1.25]	2 [2.25]
Combined therapy		
BB + CAI	20 [25.0]	19 [23.75]
BB + CAI^2	0 [0.00]	1 [1.25]
BB + PG	8[10.00]	12 [15.00]
BB + PARA	1 [1.25]	0 [0.00]
PG + CAI	1 [1.25]	1 [1.25]
BB + CAI + PG	20[25.00]	16 [20.00]
BB + CAI^2 + PG	4[5.00]	0 [0.00]
BB + CAI + PARA	1 [1.25]	2[2.25]
BB + CAI + PG + PARA	0 [0.00]	3[3.75]

BB =Beta Blocker; CAI = Carbonic anhydrase inhibitors; PG= Prostaglandins; CAI^2 = 2 Different carbonic anhydrase inhibitors; PARA = Parasympathomimetics

Table 2: Relationship between classes of drugs and therapeutic success of reduction of IOP

Class of drugs	Number of Patients	Mean ± SD IOP_1	Mean ± SD IOP_2
	Normal IOP <21mmHG		
BB	3	16 ± 7.01	11.7 ± 2.08
PG	2	21± 9.90	14 ± 4.24
BB + CAI	13	21.31 ± 9.71	15.85 ± 3.60
BB +PG	5	25.80 ± 14.03	13.40± 7.06
BB + CAI + PG	9	33 .67 ± 11.75	17 ± 2.55
BB + CAI + PARA	1	28 ± 0	7 ± 0
Multivitamins	2	13 ± 2.83	15 ± 2.83

Table 2 ***continued***

	Reduced but not normal >21mmHg		
BB	7	23.42± 6.63	26.29 ± 4.27
BB + CAI	4	27.5 ± 8.51	31.25 ± 7.18
BB +PG	2	32 ± 2.83	23.5± 0.71
PG +CAI	1	35± 0	22.00 ± 0
BB +CAI + PG	11	47.36 ± 11.60	32.64 ± 9.10
BB +CAI^2+ PG	4	49.5 ± 9.29	30.60 ± 4.35
	Failed increased IOP		
BB	5	18.20 ± 4.82	23.4 ± 5.98
BB +CAI	7	20.57 ± 9.96	24.43 ± 9.95

$IOP_{1=}$ at onset, $IOP_{2=}$ after one month, BB =Beta Blocker; CAI = Carbonic anhydrase inhibitors; PG= prostaglandins; CAI^2 = 2 Different carbonic anhydrase inhibitors; PARA = Parasympathomimetics

Table 3: Proportion of POAG patients on different classes of drugs at onset and after 1month treatment

Monotherapy	**Number of patients on it at onset [%}**	**Number of patients on it after 1 month [%]**
BB-Timolol 0.5%	9 [13.85]	6 [9.23]
BB: Betaxolol	1[1.54]	0 [0.00]
CAI: Azopt®	1[1.54]	0[0.00]
PG: Xalatan®	1[1.54]	2 [3.08]
PARA: Pilocarpine 4%	0[0.00]	1[1.54]
Multivitamins	2[3.08]	2 [3.08]
Combined therapy		
BB + CAI	17 [26.15]	17[26.15]
BB + CAI^2	0[0.00]	1[1.54]
BB + PG	7[10.77]	11[16.92]
BB + PARA	0[0.00]	[0.00]
PG + CAI	1 [1.54]	1 [1.54]
BB + CAI + PG	20 30.77]	16 [24.62]
BB + CAI^2 + PG	4 [6.15]	0[0.00]
BB + CAI + PARA	0[0.00]	0[0.00]
BB + CAI + PG + PARA	1[1.54]	2 [3.08]

BB =Beta Blocker; CAI = Carbonic anhydrase inhibitors; PG= Prostaglandins; CAI^2 = 2 Different carbonic anhydrase inhibitors; PARA = Parasympathomimetics; M/VITE = Multivitamins

Table 4: Association between demographics and classes of drugs prescribed for patients at diagnosis

Variables	Number of patients on drugs		
	Monotherapy	Combination	Total
Gender*			
Male	8	35	43
Female	12	25	37
Total	**20**	**60**	**80**
Age**			
<18 years	1	2	3
18 -34 years	3	7	9
35 -64 years	8	35	41
>65 years	8	16	24
Total	**20**	**60**	**80**
Diagnosis			
POAG	14	51	65
Ocular HTN	1	2	3
Secondary Glaucoma	2	3	5
Angle closure	0	4	4
Normal tension	3	0	3
Juvenile	0	0	0
Total	**20**	**60**	**80**

POAG-=Primary Open Angle Glaucoma, HTN= Hypertension. *P =0.1983, **P=0.789
(P< 0.05 is considered significant)

Table 5: Association between demographic and classes of drugs prescribed for POAG patients at diagnosis

Variables	Number of patients on drugs		
	Monotherapy	Combination	Total
Gender *			
Male	7	30	37
Female	7	21	28
Total	**14**	**51**	**65**
Age **			
<18 years	0	2	2
18 -34 years	1	6	7
35 -64 years	7	26	33
>65 years	6	17	21
Total	**14**	**51**	**65**

*P = 0.5611, **P = 0.789 (P< 0.05 is considered significant)

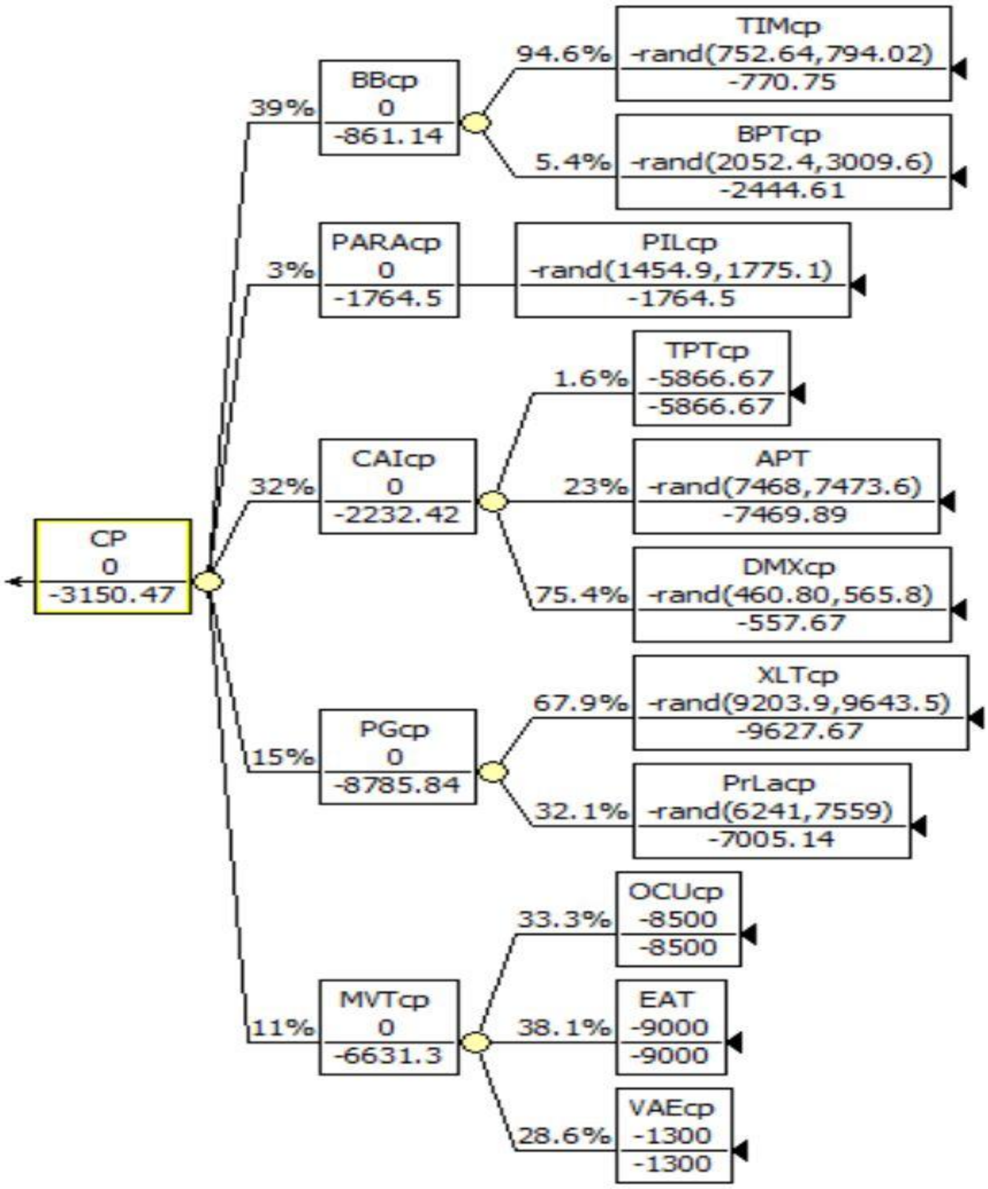

Figure 1: Model on current monotherapy practice

CP= Current Practice; BB =Beta Blocker; CAI = Carbonic anhydrase inhibitors; PG= Postagladins; PARA = Parasympathomimetics; MVT = Multivitamins; TIM = Timolol; APT= Azopt; XLT=Xalatan; PIL= Pilocarpine; OCU= Ocuvite; EAT-= Eye Anti Oxidant; VAE =Vitamin A & E; DMX = Diamox; PRL= Prostan; BPT =Beoptic. At the time of this study, $1USD was equivalent to 158.45NGN (Nigerian Naira).

After 1000 simulations, the cost-effectiveness of the current practice per month is $40.91±52.05 compared to $12.55±10.90 for the proposed POAG treatment guideline treatment for three months. This is statistically significant (P<0.0001). The current practice will cost $ 490.90 per patient per annum whereas the proposed as shown in Figure 2. POAG guidelines that result in the improved outcome will cost $50.19 thus a cost savings of $ 440.71 will be obtained by the adoption of the proposed guideline for POAG as seen in Figure 3. At the time of this study, $1 USD was equivalent to 158.45NGN (Nigerian naira).

Sensitivity analysis (figure 2) shows that the drug treatment failure rate and the cost of the prescribed combination of a beta-blocker plus carbonic anhydrase inhibitors (BBCAI) have the greatest influence on the cost-effectiveness analysis of the proposed POAG treatment guideline. Increasing the treatment failure rate or the cost of BBCAI by 50% increases the cost per patient for the three months using the proposed treatment guideline (see Figure 3) but this increase remains far less than $ 40.91which was spent per patient per month in the study site.

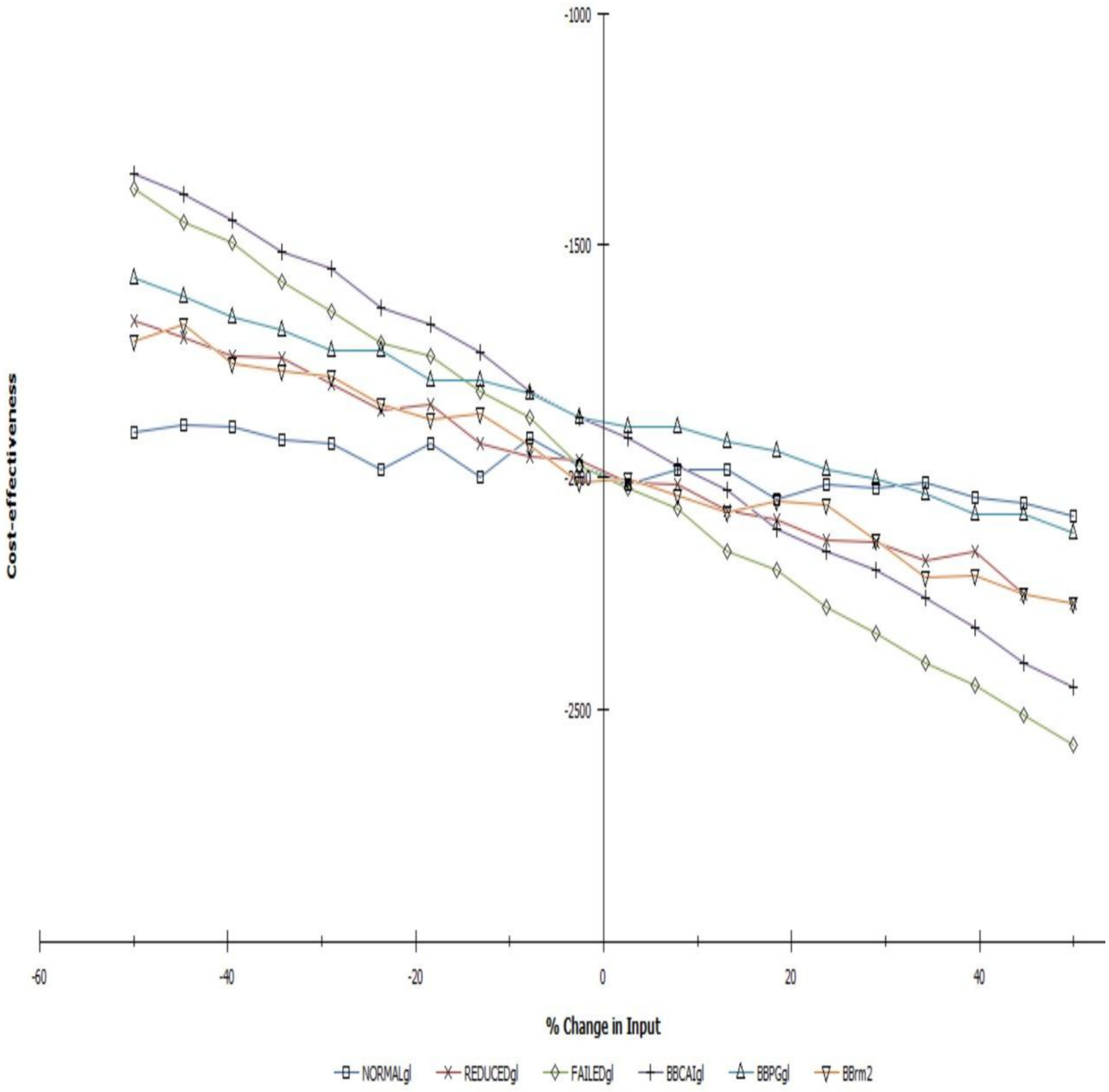

Figure 2: Sensitivity analysis of the cost effectiveness model

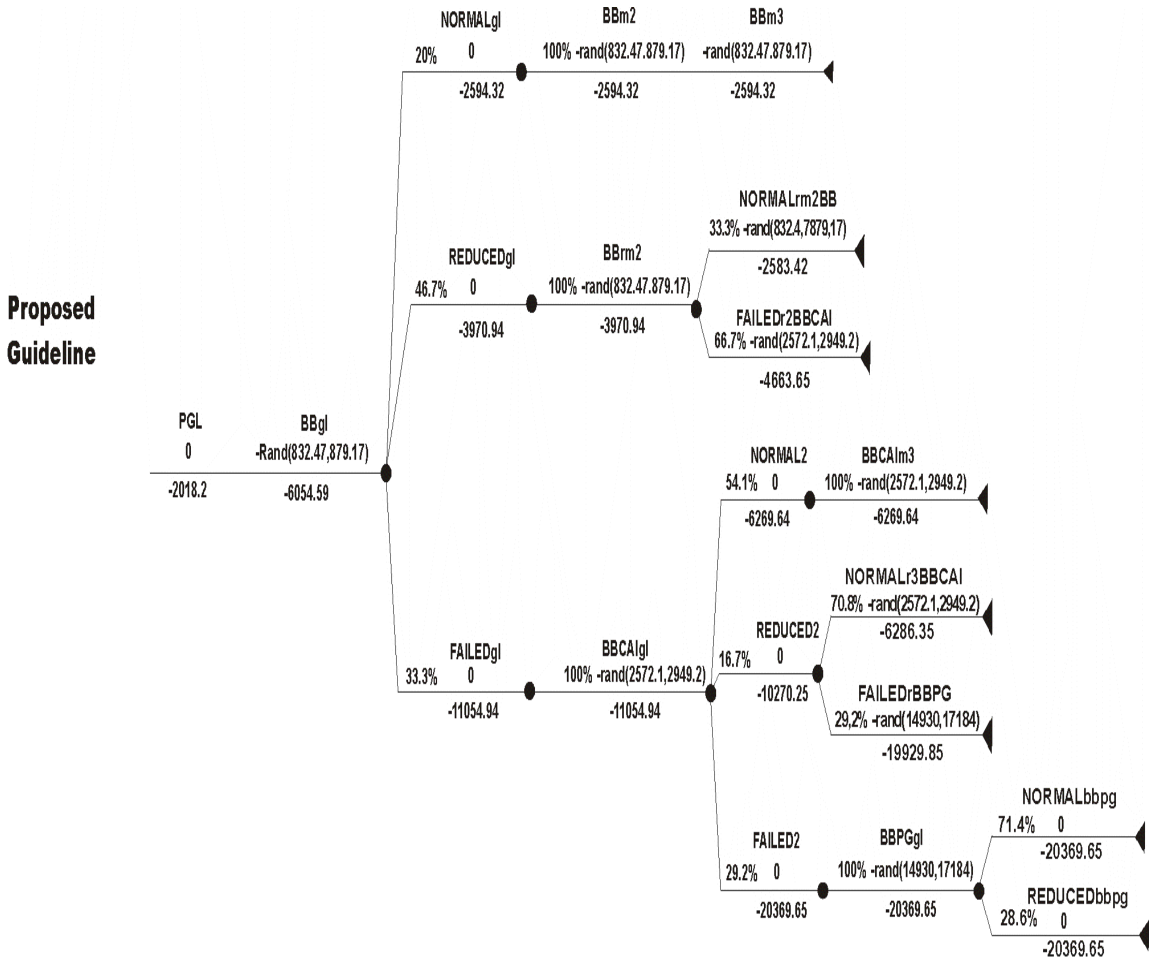

Figure 3: Model on Proposed Guideline on POAG

GL = Guideline, BB =Beta Blocker, CAI = Carbonic anhydrase inhibitors, PG= Postaglandins, PARA = Parasympathomimetics, M_2 = 2nd month, M_3 = 3rd Month. At the time of this study, \$1USD was equivalent to 158.45 NGN (Nigerian Naira)

DISCUSSION

The proportion of patients that IOP was checked regularly was low 26.76% which was contrary to glaucoma treatment guidelines [1,2] that recommended setting target IOP for different eyes/patients. This could be as a result of no standard treatment guideline for glaucoma in Nigeria at that time [7,8].

The commonly prescribed drugs were beta-blockers and carbonic anhydrase inhibitors specifically timolol and acetazolamide tablet. A high percentage of patients were on multidrug therapy at onset instead of optimizing different monotherapy to reduce side effects. We also found no association between age and sex with the type of therapy given to patients. This was similar to the study by Omoti et al. 2010 [9] where they found that the lowest annual cost of medical therapy was associated with monotherapy timolol maleate 0.5% drops, while the highest annual cost of medical therapy was related to combination therapy and prostaglandin analogues such as latanoprost 0.005% (Xalatan®) or travoprost (Travatan®), dorzolamide (Trusopt®) or brinzolamide (Azopt®) and timolol maleate 0.5% (Timoptol). Walt et al., 2004 [10] also opined that a larger percentage of patients achieved low target IOPs on bimatoprost than on latanoprost and the cost per treatment success for patients who started treatment on bimatoprost monotherapy was less compared to patients that started on latanoprost which therefore made bimatoprost more cost-effective than latanoprost based on the algorithm about clinical success at the 3- and 6-month decision points.

Cost-effectiveness should be considered along with traditional clinical safety and efficacy measures to make individual and group healthcare decisions as opined by Noecker et al., 2006 [11]. The result of this study clearly showed that the amount of money currently spent per patient in the management of POAG in the study site per month could be used to manage three patients in nine months with an improved outcome. Therefore, in the presence of limited resources, it will be more cost-effective to manage POAG using the proposed treatment guideline since not all patients experience a positive outcome despite the huge sum of money spent per patient per month as shown in the Model on guideline in Figure 2. Sensitivity analysis (figure 1) confirmed the robustness of the model since the cost-effectiveness of the proposed guideline continues to dominate current practice when input variables are adjusted by ±50%.

CONCLUSION

The prescription patterns did not follow any particular guideline as there was none in the Standard Treatment Guideline of Nigeria at the time of the study. The current practice is the use of a combination of beta-blocker and carbonic anhydrase inhibitors as first-line treatment. The model on the proposed guideline designed resulted in significant cost savings which were more cost-effective than the current practice and could be adopted after evaluation at several sites.

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