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Cost-effectiveness analysis of some medications used in the management of osteoarthritis

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Abstract
Osteoarthritis (OA) is a chronic degenerative joint disease associated with pains, disability and attendant economic effects. This study determined the cost-effectiveness of some commonly prescribed OA medications. A descriptive consecutive study was conducted in the Orthopaedic and Rheumatology Departments of the University of Benin Teaching Hospital. One hundred and twenty (120) patients diagnosed with OA were enrolled into four treatment groups of 30 patients each. Each group received diclofenac 100 mg tablets, celecoxib 200 mg capsules, tramadol 50 mg capsules and naproxen 500 mg tablets. Socio-demographic characteristics, OA severity, and prescribed medicines were documented using a structured questionnaire. Unit price of each medicine were used to estimate treatment cost. Data analysis was performed using SPSS, GraphPad Instat and Silver Decision. OA was predominant in female (30.8%), older (31.7%) and overweight (26.7%) or obese (55%) participants. Hypertension (45.8%) was the most prevalent comorbidity. Tramadol resulted in the greatest improvement (96.7%), while naproxen produced the least (53.3%) symptoms improvement. However, diclofenac and naproxen were found to be more cost-effective options. Although tramadol showed superior clinical response, diclofenac and naproxen offered better cost-effectiveness in managing knee OA, thereby underscoring the need to balance medication effectiveness with affordability.

Keywords: Cost effectiveness; Medications; Morbidity; Osteoarthritis

INTRODUCTION

Osteoarthritis (OA) is the most prevalent type of arthritis and a leading cause of pain-related disability worldwide, primarily affecting the hands, hips, knees, foot, and spine [1]. It is also known as degenerative arthritis, hypertrophic arthritis, and arthritis in the elderly. The deterioration of articular cartilage, which occurs from the interaction of several elements such as genetic, metabolic, biochemical and biomechanical, is a long-term chronic disorder that causes bones to rub against one another. The goal of OA treatment is to lessen the intensity of pain while improving function and quality of life [2,3]. Its global burden continues to rise in parallel with aging populations and increasing obesity prevalence, generating enormous direct and indirect healthcare costs.

Current international guidelines endorse a stepwise pharmacological approach in which NSAIDs are recommended as first-line agents for moderate-to-severe pain after non-pharmacological measures have proven

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insufficient [2,3]. COX-2-selective NSAIDs (coxibs) offer a comparable analgesic profile with a more favourable gastrointestinal and cardiovascular safety margin [4]. When NSAIDs are contraindicated or ineffective, opioid analgesics (including tramadol) may be considered, although their use is constrained by dependence potential, central nervous system adverse effects, and limited long-term efficacy data [5-8].

Healthcare systems, particularly in low- and middle-income countries (LMICs), operate under severe resource constraints, making it essential that prescribing choices are informed not solely by clinical efficacy but also by economic value. Cost-effectiveness analysis (CEA) provides a structured framework for comparing interventions by expressing outcomes in a common metric (typically cost per unit of health gained) thereby enabling transparent, evidence-based allocation of scarce resources [9-11].

The cost-effectiveness ratio is calculated by dividing the net cost by the changes in health outcomes. Examples include the cost per occurrence of sickness prevented or the cost per death spared. A more successful intervention is less costly, yet, if net costs are negative, the results are reported as net cost savings [12]. To compare the costs and results of alternative medical treatments, the incremental cost-effectiveness ratio (ICER) is calculated according to the formula below:

$$ICER = C_{new} - C_{old} / E_{new} - E_{old}$$

Where: ICER = incremental cost effectiveness ratio; C_{new} = cost of new healthcare; C_{old} = cost of old healthcare; E_{new} = effectiveness of new healthcare; E_{old} = effectiveness of old healthcare

Interventions with ICERs below a specified willingness-to-pay (WTP) threshold are considered cost-effective, while those exceeding the threshold, or dominated strategies that are simultaneously more costly and less effective, should not routinely be preferred [12]. Resource allocation is challenging in times of economic restraint and cannot be based only on clinical judgments, but must also take into account economic aspects [13]. Hence a careful cost-effectiveness analysis is necessary to determine which intervention to commit resources especially in the face of challenging economic realities.

This study therefore aimed to compare the cost-effectiveness of four commonly prescribed analgesic regimens for knee OA in a Nigerian tertiary hospital setting, with a view to informing rational prescribing guidelines adapted to local economic realities.

METHODS

Study design and setting. A prospective, descriptive observational study was conducted at the Orthopaedic and Rheumatology outpatient departments of the University of Benin Teaching Hospital (UBTH), a government-owned tertiary referral centre located in Egor Local Government Area, Edo State, Nigeria. UBTH serves a large, socioeconomically diverse catchment population and is representative of the tertiary healthcare context across south-south Nigeria.

Study participants/ intervention. Adult patients (≥18 years) with a physician-confirmed diagnosis of knee OA, who were consecutively prescribed one of four index analgesics—diclofenac 100 mg tablets, naproxen 500 mg tablets, tramadol 50 mg capsules, or celecoxib 200 mg capsules—were eligible for enrolment. Patients were excluded if they declined to participate, were cognitively unable to provide informed consent, or were receiving combination analgesic therapy that precluded group assignment. Participants with bilateral knee OA were instructed to respond based on the more severely affected knee.

Sample size determination. A total of 120 participants diagnosed with knee OA were recruited conveniently for the study and liberally assigned into four treatment groups,

with thirty patients blindly assigned to each group reflecting routine clinical prescribing rather than experimental randomization. A sample of 30 per group was considered sufficient to detect clinically meaningful within-group changes in Lequesne Index scores based on previous investigations in comparable populations [14].

Sampling technique. A purposive sampling technique was used to recruit patients who met the inclusion criteria and were prescribed one of the investigated medications for knee osteoarthritis during the study period.

Consent to participate. All eligible patients were informed about the objectives of the study, assured of anonymity, and written informed consent was obtained prior to participation.

Ethical approval. Ethical approval for the study was obtained from the Research and Ethics committee of the University of Benin Teaching Hospital (UBTH) with approval number ADM/E 22/A/VOL. VII/14783. All procedures were conducted in accordance with institutional ethical standards.

Instruments, data collection and time horizon. A structured, interviewer-administered questionnaire was used to capture: (i) socio-demographic characteristics (age, sex, body mass index [BMI], marital status, educational attainment, health insurance coverage, smoking and alcohol use, clinical data including comorbid conditions and family history of OA; and (iii) prescribed analgesic and dose. For participants with limited literacy, questionnaire items were read aloud and explained in the patient's preferred language. Knee OA severity was assessed at baseline and after three weeks of treatment using the Lequesne Algofunctional Index of severity for knee OA [14], a validated, 11-item instrument covering three domains: (a) pain and discomfort, (b) maximum walking distance, and (c) activities of daily living. Composite scores were categorised as: 0 = none; 1–4 = mild; 5–7 = moderately severe; 8–10 = severe; 11–13 = very severe; ≥14 = extremely severe. Internal consistency of the scale in this sample was assessed using Cronbach's alpha, and dimensionality was examined by exploratory factor analysis with varimax rotation.

Health outcomes. Health outcomes were assessed by comparing knee OA severity at baseline and after three weeks of treatment. The difference in scores provided a measure of treatment benefit.

Cost estimation. The cost of each analgesic regimen was estimated from the unit price (cost per tablet or capsule) of each dosage form, multiplied by the prescribed quantity over the three-week period. Unit prices were obtained from the UBTH pharmacy department and represent actual patient-incurred acquisition costs in Nigerian Naira (NGN) at the time of the study. Costs were evaluated from the patient perspective, consistent with the predominantly out-of-pocket financing structure of healthcare in Nigeria. Indirect costs (e.g., transportation, lost productivity) and healthcare provider costs were not captured given the observational design.

Cost-effectiveness analysis. Cost-effectiveness analysis was conducted using the Silver Decision analytical software, which implements a probabilistic decision-tree model using the cost and effect data of the prescribed medications. See figure 1. For each treatment arm, 1,000 Monte Carlo simulations were performed by sampling from the observed distributions of cost and effect, yielding mean cost-effectiveness ratios (CERs) with standard deviations. The CER for each drug was expressed as the cost per unit improvement in Lequesne Index score (NGN per effect unit). Incremental cost-effectiveness ratios (ICERs) were computed by ranking treatments in ascending order of cost and sequentially comparing each strategy with the next less

costly alternative. Results were summarized in a league table [15] as shown in figure 2, with dominated strategies (those exhibiting higher cost and lower effect than a comparator) identified and excluded from the efficiency frontier.

Data analysis. Descriptive statistics were reported as frequencies and percentages for categorical variables. Associations between socio-demographic characteristics and OA severity (before and after treatment) were assessed using the chi-square test, with significance set at $P \leq 0.05$. All descriptive and inferential analyses were performed in SPSS version 22.0 (IBM Corp., Armonk, NY, USA) and GraphPad InStat. CEA modelling was conducted in Silver Decision. Reliability of the 11-item questionnaire was assessed by using Cronbach's alpha**,** factor loading was done using varimax rotation with Kaiser normalization to explore internal consistency.

RESULTS

The Cronbach's alpha and factor loading were 0.89 and 0.76 respectively.

Socio-demographic data of participants. The socio-demographic characteristics of the 120 participants are summarized below in table 1. Knee OA was predominant among female (n = 83; 69.2%) and individuals aged 60 – 69 years (n = 38; 31.7%). Most of the participants were overweight (26.7%) and obese (55%). In terms of education, 47 participants (39.2%) had secondary education, while 4 (3.33) had no formal education. Only 25% of the participants had health insurance coverage, and 56.7% reported a family history of OA. Hypertension was the predominant comorbidity (n=55, 45.8%). Smoking and alcohol consumption were reported by 23.3% and 30% of the participants, respectively.

Changes in OA severity following pharmacotherapy. Table 2 presents the distribution of Lequesne severity scores before and after three weeks of treatment. At baseline, the majority of participants across all four groups were classified as having extremely severe OA (37.5%), severe OA (29.2%), or very severe OA (20.8%). Following treatment, the proportion classified as mild increased markedly in all groups: diclofenac (3.3% → 83.3%), naproxen (3.3% → 53.3%), tramadol (0.0% → 96.7%), and celecoxib (3.3% → 56.7%). The elimination of the extremely severe and severe categories post-treatment was observed across all arms. Statistically significant within-group improvements were recorded for tramadol ($P = 0.001$) and naproxen ($P = 0.027$). Improvements in the diclofenac and celecoxib groups, while clinically substantial, did not reach statistical significance ($P = 0.066$ and $P = 0.069$, respectively).

Influence of socio-demographic factors on disease severity and response to pharmacotherapy. Before treatment, higher severity scores were observed among female patients, those aged 50–69 years, participants with obesity, and those with hypertension as a comorbidity. Smokers and alcohol consumers also exhibited greater disease severity than their counterparts. However, none of these associations reached statistical significance at the $P \leq 0.05$ threshold (Table 3), suggesting that confounding by group-level heterogeneity may have limited statistical power in this sample. After treatment, better therapeutic responses were observed among male patients, participants of normal weight (BMI 18.5–24.9 kg/m²), those aged 40–49 years, and individuals with a history of peptic ulcer disease. Non-smokers and non-alcohol users demonstrated relatively superior post-treatment outcomes (Table 4). Nonetheless, none of these differential responses were statistically significant, precluding definitive subgroup conclusions.

Cost effectiveness analysis. Figure 1 shows the Silver decision analytical software decision tree output for the computation of the cost effectiveness ratios while Figure 2 shows the league table comparing the cost-effectiveness of the four medications. Treatment with celecoxib and tramadol incurred a higher cost per unit of outcome compared with diclofenac and naproxen. As a result, both celecoxib and tramadol were dominated alternatives.

Table 1: Socio-demographic data (N=120)

Variable	Class	Frequency	Percentage (%)
Gender	Male	37	30.8
	Female	83	69.2
Age (years)	30-39	2	1.7
	40-49	17	14.2
	50-59	35	29.2
	60-69	38	31.7
	70-79	21	17.5
	≥80	7	5.8
BMI (kg/m^2)	<18.5	1	0.8
	18.5-24.9	21	17.5
	25-29.9	32	26.7
	>30	66	55
Marital Status	Married	97	80.8
	Single	2	1.7
	Divorced	2	1.7
	Widowed	16	13.3
	Separated	3	2.5
Education	No education	4	3.33
	Pri. Education	35	29.2
	Sec. Education	47	39.2
	Tert. Education	34	28.3
Health Insurance	Yes	30	25
	No	90	75
Family History	Yes	68	56.7
	No	52	43.3
Co-morbid Disease	Diabetes	24	20
	Hypertension	55	45.8
	Ulcer	27	22.5
	Asthma	14	11.7
Smoking	Yes	28	23.3
	No	92	76.7
Alcohol	Yes	36	30
	No	84	70

Table 2: Frequency distribution of OA severity before and after treatment with different medications. (N=120)

Level of severity	Severity before and after treatment with different medications								Total (%)	
	Diclofenac 50 mg (n=30)		Naproxen 500 mg (n=30)		Tramadol 50 mg (n=30)		Celecoxib 200 mg (n=30)			
	Before (%)	After (%)	Before (%)	After (%)	Before (%)	After (%)	Before (%)	After (%)	Before	After
Extremely severe	11 (37)	0 (0)	10 (33.3)	0 (0)	11 (37)	0 (0)	13 (43.3)	0 (0)	45(37.5)	0(0)
Very severe	6 (20)	0 (0)	6 (20)	0 (0)	6 (20)	0 (0)	7 (23.3)	1(3.3)	25(20.8)	1(0.8)
Severe	10 (33.3)	0 (0)	8 (26.7)	0 (0)	9 (30)	0 (0)	8 (26.7)	0 (0)	35(29.2)	0(0)
Moderately severe	2 (7)	5 (16.7)	5 (16.7)	14 (46.7)	4 (13.3)	1 (3.3)	1 (3.3)	12 (40)	12(10.0)	33(27.5)
Mild	1 (3.3)	25 (83.3)	1 (3.3)	16 (53.3)	0 (0)	29 (96.7)	1 (3.3)	17 (56.7)	3(2.5)	86(71.7)
P-value	0.0657		0.0268		0.001		0.0694			

Table 3: Effect of socio-demographic data on OA severity before pharmacotherapy (N=120)

Demographic data		Level of severity				
Variable	Class	Extremely severe	Severe	Mild	Total	P-value
Gender	Male	18(48.6)	15(40.5)	4(10.8)	37	0.1869
	Female	52(62.7)	20(24.1)	11(13.3)	83	
Age	<50	42(52.6)	5(26.3)	4(21.1)	19	0.8942
	50-69	42(57.5)	22(30.1)	9(12.3)	73	
	≥70	18(64.3)	8(28.6)	5(17.86)	28	
BMI	<24.9	10(45.5)	9(40.9)	3(13.6)	22	0.5529
	25-29.9	29(90.6)	18(56.3)	6(18.8)	32	
	≥30	42(63.6)	16(24.2)	9(13.6)	66	
Family history	Yes	43(63.2)	18(26.5)	7(10.3)	68	0.2778
	No	27(52.0)	7(13.5)	8(15.4)	52	
Co-morbid condition	Diabetes	12(50)	9(37.5)	3(12.5)	24	0.1149
	Hypertension	39(70.9)	10(18.2)	6(10.9)	55	
	Ulcer	14(51.85)	11(40.7)	2(7.4)	27	
	Asthma	6(42.9)	4(28.6)	4(28.6)	14	
Smoking	Yes	19(67.9)	6(21.4)	3(10.7)	28	0.4939
	No	51(55.4)	29(31.5)	12(13)	92	
Alcohol	Yes	23(63.9)	9(25)	4(11.1)	36	0.7198
	No	47(56)	26(31)	11(13.1)	84	

Table 5: Incremental cost-effectiveness ratio (ICER) after 1000 simulations

Drugs	Price (NGN) ± SD	Effect score ± SD	CER (NGN) ± SD
Diclofenac 100mg	360.70 ± 103.81	3.00 ± 0.87	132.157 ± 59.51
Naproxen 500mg	1783.19 ± 533.30	2.67 ± 0.78	733.32 ± 328.08
Tramadol 50mg	2468.64 ±720.73	3.11 ± 0.90	878.27 ± 403.67
Celecoxib 200mg	2705.52 ± 769.77	2.85 ± 0.80	1042.24 ± 459.63
P-Value	0.0001	0.0001	0.0001

Table 4: Effect of socio demographic data on OA severity.

Demographic data		Level of severity					
Variable	Class	Extremely severe	Very severe	Severe	Moderately severe	Mild	Total
Gender	Male	0 (0)	0 (0)	0 (0)	8 (22)	29 (78)	37
	Female	0 (0)	1 (1.2)	0 (0)	24 (28.9)	58 (69.9)	83
Age	<30	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0
	30-39	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	2
	40-49	0 (0)	0 (0)	0 (0)	3 (17.6)	14 (82.4)	17
	50-59	0 (0)	0 (0)	0 (0)	13 (37.1)	22 (62.9)	35
	60-69	0 (0)	1 (2.6)	0 (0)	7 (18.4)	30 (78.9)	38
	70-79	0 (0)	0 (0)	0 (0)	6 (28.6)	15 (71.4)	21
	≥80	0 (0)	0 (0)	0 (0)	2 (28.6)	5 (71.4)	7
BMI	<18.5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0
	18.5-24.9	0 (0)	0 (0)	0 (0)	3 (14.3)	18 (85.8)	21
	25-29.9	0 (0)	1 (3.1)	0 (0)	10 (31.3)	21 (65.6)	32
	≥30	0 (0)	0 (0)	0 (0)	19 (28.4)	48 (71.6)	67
Family history	Yes	0 (0)	1 (1.47)	0 (0)	17 (25)	50 (73.5)	68
	No	0 (0)	0 (0)	0 (0)	15 (28.5)	37 (71.2)	52
Co-morbid condition	Diabetes	0 (0)	0 (0)	0 (0)	8 (26.7)	22 (73)	30
	Hypertension	0 (0)	0 (0)	0 (0)	20 (30.8)	45 (69.2)	65
	Ulcer	0 (0)	1 (6.7)	0 (0)	1 (6.7)	13 (86.7)	15
	Asthma	0 (0)	0 (0)	0 (0)	3 (30)	7 (70)	10
Smoking	Yes	0 (0)	0 (0)	0 (0)	12 (43)	16 (57.1)	28
	No	0 (0)	1 (1.1)	0 (0)	20 (21.7)	71 (77.2)	92
Alcohol	Yes	0 (0)	1 (2.8)	0 (0)	11 (30.6)	24 (66.7)	36
	No	0 (0)	0 (0)	0 (0)	21 (25)	63 (75)	84

OA severity after pharmacotherapy (N=120)

TABLE 5: Incremental cost-effectiveness ratio (ICER) after 1000 simulations

Drugs	Price (NGN) ± SD	Effect score ± SD	CER (NGN) ± SD	Rank
Diclofenac 100mg	360.70 ± 103.81	3.00 ± 0.87	132.157 ± 59.51	1st
Naproxen 500mg	1783.19 ± 533.30	2.67 ± 0.78	733.32 ± 328.08	2nd
Tramadol 50mg	2468.64 ±720.73	3.11 ± 0.90	878.27 ± 403.67	3rd *
Celecoxib 200mg	2705.52 ± 769.77	2.85 ± 0.80	1042.24 ± 459.63	4th *
P-Value	0.0001	0.0001	0.0001	

*CER = cost-effectiveness ratio; NGN = Nigerian Naira; SD = standard deviation. * Dominated strategy (higher cost and/or lower effect relative to a comparator on the efficiency frontier). Ranks reflect ascending CER.*

Table 5 presents the results of the probabilistic CEA after 1,000 Monte Carlo simulations generated from figures 1 and 2. Diclofenac 100 mg was by far the least expensive regimen (mean cost: NGN 360.70 ± 103.81), while celecoxib was the most expensive (NGN 2,705.52 ± 769.77). Tramadol produced the largest mean effect score (3.11 ± 0.90 units), marginally exceeding diclofenac (3.00 ± 0.87 units). Despite this, diclofenac achieved the lowest CER (NGN 132.16 ± 59.51 per effect unit), establishing it as the dominant treatment on the cost-effectiveness frontier. Naproxen ranked second (CER: NGN 733.32 ± 328.08), while tramadol (CER: NGN 878.27 ± 403.67) and celecoxib (CER: NGN 1,042.24 ± 459.63) were dominated strategies — incurring disproportionately higher costs relative to the clinical benefit conferred. The decision tree (Figure 1) and the league table (Figure 2) consistently identified diclofenac and naproxen as the preferred options on economic grounds hence ranked 1st and 2nd respectively as shown in Table 5. Price differences, effect scores, and CERs across treatments were all statistically significant ($P < 0.0001$).

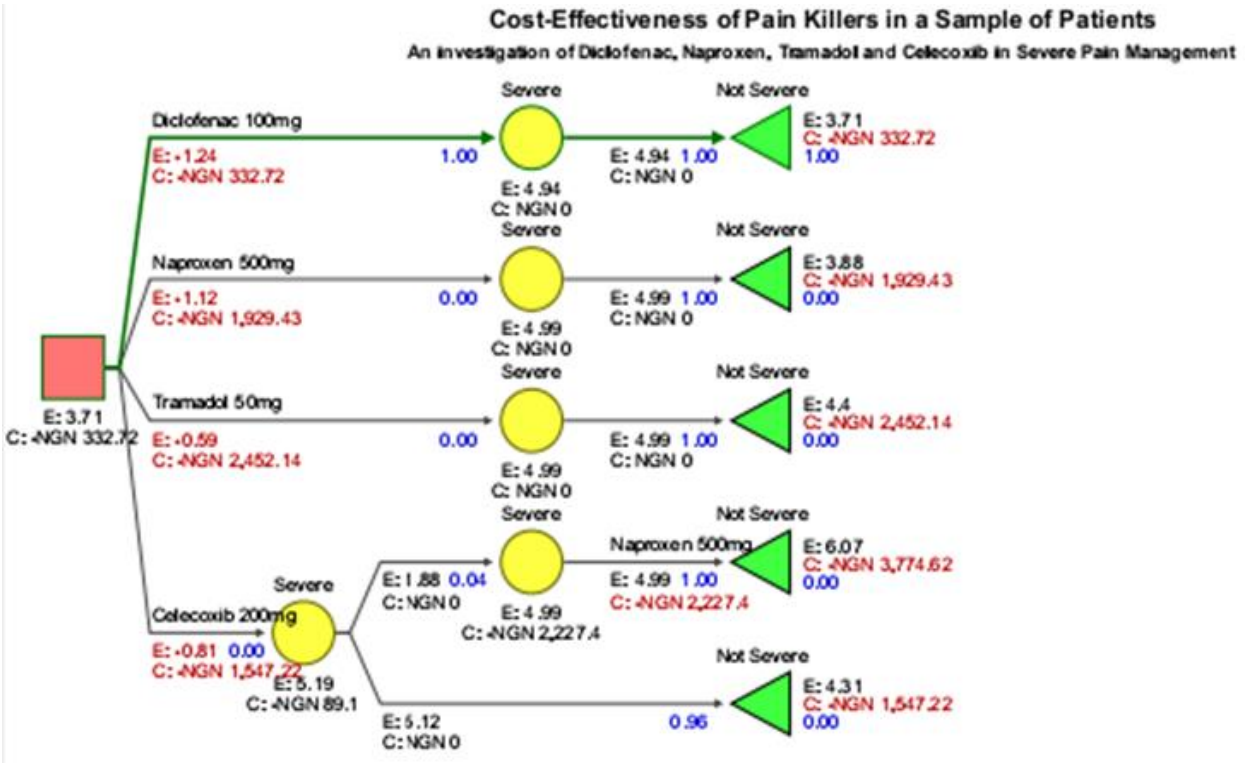

Figure 1: Decision tree used for Cost effectiveness analysis of prescribed pain killers in study participants. The thick line indicates that diclofenac 100mg is more cost effective

League table

Policy #	Policy	Effect	Cost	Comment
1	:Celecoxib 200mg	2.2549819973717957	-4022.6127945651456	dominated (by #3)
2	:Tramadol 50mg	2.487063556771679	-2641.24391905629	dominated (by #3)
3	:Diclofenac 100mg	2.605320357464048	-180.52273288420162	incremental ratio=0
4	:Naproxen 500mg	2.789306344674765	-1230.5038508166376	incremental ratio=5706.85373299599

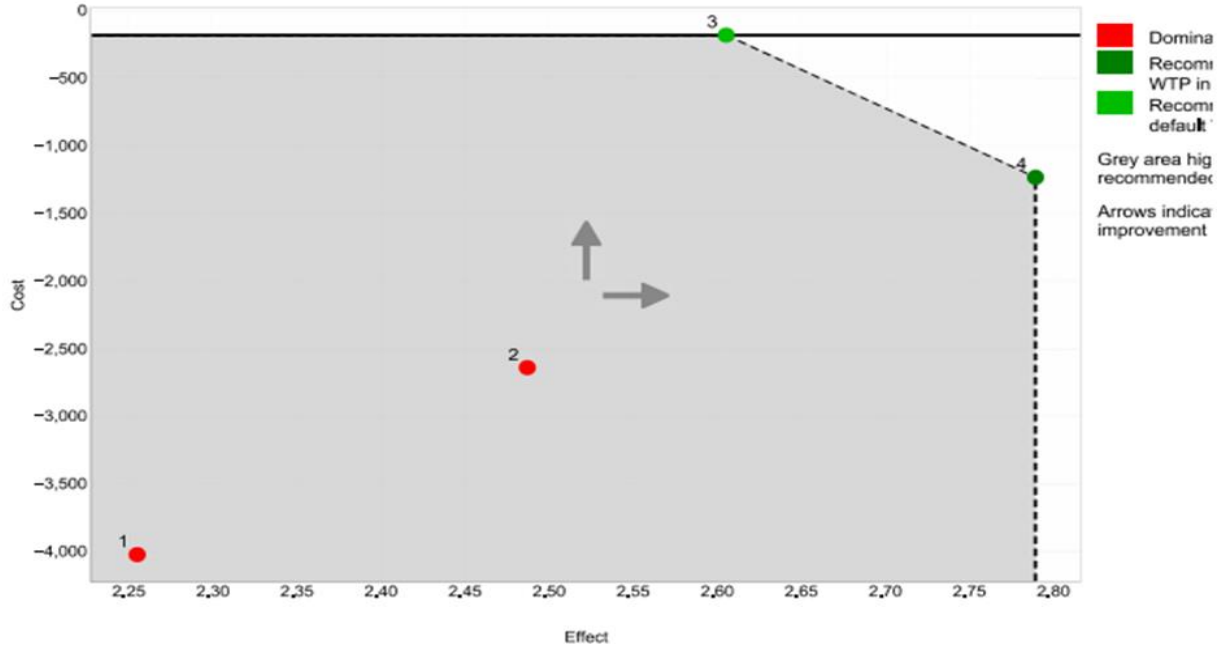

Figure 2: League table comparing the cost-effectiveness of diclofenac, tramadol, naproxen and celecoxib

DISCUSSION

Osteoarthritis (OA) is the most frequent form of arthritis worldwide and a leading cause of disability among older adults [16]. The goal of treatment in OA is to reduce pain intensity and improve function and quality of life through a combination of non-pharmacological and pharmacological interventions [16]. According to several treatment guidelines the first-line medications for the treatment of OA is NSAIDs [17, 18]. However, the healthcare landscape is characterized by a diverse range of treatment options, technologies, and interventions, each with varying levels of effectiveness and cost.

It is important to assess the cost and outcomes of different interventions. This will enable clinicians and prescribers to take informed decision when recommending medications. In order to carry out a cost-effectiveness analysis, measures of effectiveness (outcomes) must be comparable. These will depend on the objectives of the particular interventions that are being studied. In all cost-effectiveness analysis, however, measures of effectiveness should be defined in appropriate natural units and expressed in a single dimension.

This study measures the outcomes of interventions based on their ability to reduce OA severity determined by lequesne algofunctional index of severity of knee OA. It provides cost-effectiveness evidence for four analgesic regimens used in the management of

knee OA within a Nigerian tertiary care hospital — a context characterised by high out-of-pocket healthcare expenditure, limited health insurance coverage, and escalating pharmaceutical costs.

The principal finding is that diclofenac 100 mg is the dominant, most cost-effective option, yielding a CER approximately 5.5-fold lower than naproxen and 6.6-fold lower than tramadol. These results have direct relevance for prescribing practices in resource-constrained LMICs where economic considerations must necessarily accompany clinical decision-making. Also, women preponderance for more severe cases of OA – finding buttressed by previous studies [19, 20] - was evident. This might be due to women's weaker muscles, less cartilage volume, or bone loss [21]. Patients between the ages of 50 and 69 had a higher prevalence and severity of the disease condition. Given that age is thought to be a significant contributing factor to the deterioration of knee articular structures, this may be related to age over time [22]. Obesity, regarded as one of the most potent and well-known risk factor for osteoarthritis [23, 24], was highly prevalent as the majority of patients in this study were overweight (BMI=25–29.9 kg/m2) or obese (BMI≥30 kg/m²). This supports the conclusions of a number of researches [25, 26]. Hypertension was the most frequent comorbidity (45.8%), a finding of clinical relevance because it limits the safe use of NSAIDs due to their propensity to elevate blood pressure, impair renal function, and interact with antihypertensive agents particularly in older patients [17,18]. This observation reinforces the importance of individualising analgesic selection rather than applying a uniform first-line NSAID strategy.

Due to the risk of dependence and toxicity [27] opioids are not commonly recommended in the management of osteoarthritis. The American College of Rheumatology (ACR) suggests using opioids in patients who have failed all other pharmacologic treatments and are unwilling to undergo or are contraindicated for total knee arthroplasty (TKA) [28]. All four regimens produced clinically meaningful reductions in Lequesne severity scores over three weeks. Tramadol achieved the highest proportional improvement rate (96.7%), in keeping with evidence from systematic reviews demonstrating that opioids provide statistically greater pain relief than placebo in hip and knee OA, particularly for severe baseline pain [7]. The more modest improvement observed with naproxen (53.3%) may partly reflect its pharmacodynamic profile, as naproxen's longer half-life and relatively lower peak plasma concentration may confer less pronounced acute analgesic effect compared with tramadol's central opioid mechanism. Diclofenac's 83.3% improvement rate is noteworthy and consistent with its established efficacy as a potent dual COX-1/COX-2 inhibitor with additional central analgesic properties [4].

The divergence between clinical and economic rankings is the central and clinically actionable finding of this study. Although tramadol produced the largest absolute reduction in OA severity, it was a dominated strategy: its CER of NGN 878.27 per effect unit was approximately 6.6 times higher than that of diclofenac. The critical driver of this result is the profound price differential between diclofenac (NGN 360.70 per treatment course) and tramadol (NGN 2,468.64), which far outweighs tramadol's marginal additional effectiveness advantage [29]. Hence, tramadol and celecoxib were dominated. Similar conclusions have been reached in published cost-effectiveness models from high-income settings: Katz et al. [30] demonstrated that opioids, including tramadol and oxycodone, were not cost-effective relative to NSAIDs for knee OA management across a range of willingness-to-pay thresholds in older patients with comorbidities. Prescriber familiarity, patient preference for perceived

potency and effectiveness of tramadol could be responsible for its increased use in OA management not minding the associated drawbacks which include higher cost of treatment, toxicities, frequent monitoring, reduced efficacy of eventual total knee arthroplasty, and risk of illicit use [31]. Diclofenac which is considerably cheaper in price was found to be more cost effective. Celecoxib was similarly dominated, with the highest CER of all four agents (NGN 1,042.24 per effect unit) and approximately a 7.9-fold cost disadvantage relative to diclofenac. While celecoxib's selective COX-2 inhibition offers a superior gastrointestinal safety profile compared with non-selective NSAIDs, this pharmacological advantage is not captured in the current cost-effectiveness model, which focused exclusively on analgesic effectiveness. Clinicians managing high-risk patients (e.g., those with a history of peptic ulcer disease, concomitant anticoagulant use, or advanced age) may appropriately choose celecoxib despite its higher CER, recognising that a broader cost perspective encompassing adverse event-related costs may alter the relative ranking. Future analyses incorporating safety costs and quality-adjusted outcomes would enrich the evidence base.

This brings to mind that apart from benefits, cost considerations are usually very important when deciding which intervention to commit scarce healthcare resources [32]. Given a consistent rise in health care cost, available resources must be allocated judiciously so as to ensure optimization of limited resources, ensure interventions provide proportionate benefits for their cost, and guiding policy decisions by allowing comparison between different treatments and public health strategies.

Conclusion. This prospective observational study demonstrates that all four analgesic regimens - diclofenac, naproxen, tramadol, and celecoxib - produced clinically meaningful improvements in knee OA severity over three weeks. Tramadol achieved the greatest proportional symptom reduction; however, its substantially higher cost per unit of benefit rendered it a dominated strategy. Diclofenac 100 mg emerged as the most cost-effective option for knee OA management in this Nigerian tertiary care setting, offering the lowest cost-effectiveness ratio and remaining the recommended first-line agent consistent with international guidelines. Naproxen was the second most cost-effective alternative.

These findings underscore the imperative of embedding pharmacoeconomic evidence into clinical decision-making and formulary policy, particularly in healthcare systems where out-of-pocket costs represent a significant barrier to equitable access. Policymakers and clinicians in sub-Saharan Africa and comparable LMIC settings should consider cost-effectiveness alongside clinical efficacy when developing analgesic prescribing protocols for osteoarthritis.

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