This study aimed at describing the cost-effectiveness of four regimen commonly employed in Enugu State, Nigeria for eradicating Helicobacter pylori. A decision analysis model was constructed to represent the strategies used in eradication of H. pylori in most practice setting in Enugu State. Each of the four strategies was hypothesized to have been administered to a cohort of 100 patients. Cost of medication was the only cost component included and were based on 2007 prices. Base estimates for eradication of H. pylori with omeprazole, clarithromycin and metronidazole (OCM), omeprazole, amoxicillin and metronidazole (OAM), and re-treatment with OCM were obtained from an earlier published study. The average cost-effectiveness ratio was determined. Incremental costs of the strategy with highest effectiveness in relation to other strategies were also calculated. The unit of comparison for evaluating cost-effectiveness was the number of years it would take for the cumulative future cost of treating a patient with relapse treatment, to equal the incremental cost of the most effective eradication therapy. The use of OAM in eradication of H. pylori in patients with duodenal ulcer and re-treating with OCM in patients that still shows dyspeptic symptoms is the most cost-effective option compared to the other three strategies.

Keywords: Decision analysis; duodenal ulcer; cost-effectiveness; Helicobacter pylori.

INTRODUCTION
Helicobacter pylorus is ubiquitous in Africa, with acquisition in childhood the rule. It has been established that most patients with a duodenal ulcer and many with gastric ulcers are colonized with H. pylori. As a result, many investigators have divided peptic ulcer disease into three etiologic groups based on pathophysiological abnormalities and they include: (1) ulcers associated with H. pylori infection, (2) those caused by NSAID use, and (3) those with acid hypersecretion. Patients who remain positive for H. pylori have a higher recurrence rate within the first year after healing compared with patients in whom eradication of H. pylori is achieved. Over a 6- to 12-month period following initial ulcer healing, ulcer recurrence rates have been documented to be 85% in H. pylori-positive patients, but only 10% in H. pylori-negative patients. Thus, H. pylori eradication therapy is recommended for all H. pylori-positive patients with confirmed gastric or duodenal ulcers, both patients presenting with first ulcers and those presenting with recurrence.

Monotherapy with antibiotics or with acid suppressants has not been optimal and thus, combination therapies consisting of antibiotics and suppressants (Proton pump inhibitors or H₂-receptor antagonists) have become the primary mainstays in the management of H. pylori positive ulcer patients. However, different eradication regimens have dissimilar efficacy and wide variation in cost. Use of cost-effective regimen in the treatment of ulcer patients would result in resource savings for patients and would ensure efficient distribution of health resources. This study is an economic evaluation aimed at describing the cost-effectiveness of four eradication regimen commonly employed in Enugu, a state in South-Eastern Nigeria for eradicating Helicobacter pylori, using a hypothetical cohort of 100 patients.

METHODS
Decision analysis model
The model was constructed to represent the strategies used in eradication of Helicobacter pylori in most practice settings in Enugu State. Interview with five consultant gastroenterologists practicing in Enugu revealed that patients with clinical symptoms of ulcer are normally placed on Helicobacter pylori eradication regimen presumptively without any confirmatory test. Patients are monitored and if dyspeptic symptoms persist or reappear, they are given another course of eradication regimen or managed with H₂ receptor antagonist or proton pump inhibitors. Helicobacter pylori eradication regimen often made use of are omeprazole, clarithromycin, and metronidazole and omeprazole, amoxicillin, and metronidazole. Thus, a decision analysis model was constructed employing a simple decision tree to model four different strategies of eradicating Helicobacter pylori in patients with duodenal...
ulcer (Figure 1). The strategies used in the model included:

- **Strategy 1**: omeprazole (20mg) twice daily, amoxicillin (1g) twice daily, and metronidazole (400mg) twice daily, all for 7 days (OAM 7 days).
- **Strategy 2**: omeprazole (20mg) twice daily, clarithromycin (250mg) twice daily, and metronidazole (400mg) twice daily, all for 7 days (OCM 7 days).
- **Strategy 3**: Strategy 1 plus repeat therapy with omeprazole (20mg) twice daily, clarithromycin (250mg) twice daily, and metronidazole (400mg) twice daily, all for 7 days.
- **Strategy 4**: Strategy 2 plus repeat with omeprazole (20mg) twice daily, clarithromycin (250mg) twice daily, and metronidazole (400mg) twice daily, all for 7 days.

Patients in whom eradication treatment was unsuccessful would only have treatment for acid suppression with ranitidine (150mg), a H₂ receptor antagonist twice daily for 6 weeks, if they had recurrent ulcers that produced symptoms. Decision analysis was based on DATA software (version 3.5; Treeage Software, Williamstown, MA).

**Efficacy indicator**

Base estimates for eradication of *Helicobacter pylori* with omeprazole, clarithromycin and metronidazole (OCM), omeprazole, amoxicillin and metronidazole (OAM), and re-treatment with OCM were obtained from an earlier published study. In the study, estimates for the eradication of *H. pylori* with each regimen and the 95% confidence intervals were obtained by calculating the mean eradication rates of *Helicobacter pylori* from published non-randomised trials up to November 1995. For the OCM regimen there were 15 trials with a total of 1125 patients, with an overall eradication rate of 91%, and for the OAM regimen there were 4 trials with a total of 673 patients and an overall eradication rate of 85%. Estimates for the eradication of *H pylori* with a repeat therapy with omeprazole, clarithromycin, and metronidazole (OCM 7 days) after initial failure with either regimen were obtained by calculating the mean eradication rate of *H. pylori* using the regimen in patients who had failed eradication treatment from all trials up to October 1996. Details of the efficacy estimates used in the study are shown in Table 1.

**Table 1: Efficacy and cost estimates of different strategies for eradication of *H. pylori* in Enugu State**

<table>
<thead>
<tr>
<th>Table 1: Efficacy and cost estimates of different strategies for eradication of <em>H. pylori</em> in Enugu State</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable</strong></td>
</tr>
<tr>
<td>Radiation regimen (%)</td>
</tr>
<tr>
<td>Omeprazole, clarithromycin, metronidazole (7 days)</td>
</tr>
<tr>
<td>Omeprazole, amoxicillin, metronidazole (7 days)</td>
</tr>
<tr>
<td>Repeat therapy with omeprazole, clarithromycin, metronidazole (7 days)</td>
</tr>
</tbody>
</table>

†Estimates of eradication rates were obtained from Duggan et al, 1998

*Cost data were obtained from Central medical store, Enugu State

NB: US$1.00 is equivalent to ₦120.00

**Cost data**

Cost effectiveness was conducted from the perspective of the providers. Cost per patient assessment included the cost of omeprazole, clarithromycin and metronidazole, omeprazole, amoxicillin and metronidazole regimens, and the yearly cost of relapse treatment of duodenal ulcer disease with ranitidine 150mg twice daily for 4 weeks. Since indication for eradication of *H. pylori* is based on presumptive treatment and no confirmatory test conducted, only drug costs were used. Treatment for relapse was assumed to last for 6 weeks, and each patient that experienced failure with any of the eradication strategy would receive relapse treatment twice a year.

**Cost effectiveness analysis**

Hundred patients with duodenal ulcer, positive for *Helicobacter pylori* were assumed to be treated with each of the four strategies. The decision model explored the cost in eradicating *Helicobacter pylori* in these patients. For each successful *Helicobacter pylori* eradication, the average patient cost (ACER) was calculated with the formula below:
However, the strategy with the highest efficacy would be OCM, OCM alone, and finally OCM plus repeat OCM. OAM alone had the least ACER followed by OAM plus repeat OCM. Using OAM to eradicate H. pylori will consume the least amount of resources. Eradication of H. pylori with ranitidine 150mg twice daily for 4 weeks duration given once yearly. The unit of comparison for evaluating cost effectiveness was the number of years it would take for the future cost of treating a patient with relapse treatment, to equal the incremental cost of the most effective eradication therapy.

### Sensitivity analysis

Sensitivity analysis was used to test the CEA results to parameter alteration. Ranges of eradication rate estimates were used to perform one-way sensitivity analysis. The minimum and maximum cost of medications of the different eradication strategies were used in a multi-way sensitivity analysis to test the impact of price variation on the results obtained in the original analysis.

### RESULTS

The differences in cost and efficacy outcome between the four H. pylori eradication strategies are described in Table 2. Considering only the cost of medication, using OAM to eradicate H. pylori will consume the least resources but also has the least efficacy (Strategy 2). Using OCM and repeating the same treatment in patients that had eradication failure (Strategy 3) would have the highest efficacy but also would consume the largest amount of resources. Eradication of H. pylori with OCM without repeat treatment (Strategy 1) has the second highest cost and efficacy. Using OAM plus repeat treatment with OCM for patients in whom eradication of H. pylori was unsuccessful (Strategy 4) would amount to a higher cost compared to OAM alone.

Average cost effective ratios (ACER) were also determined. ACER estimates the cost per successful eradication of H. pylori infection. Lower ACER signifies a more preferred strategy since a low resource input is consumed for each successful eradication. Using OAM alone had the least ACER followed by OAM plus repeat OCM, OCM alone, and finally OCM plus repeat OCM. However, the strategy with the highest efficacy would be preferred since many patients would be relieved of ulcer. In this analysis, we sought to describe the best alternative to the eradication strategy with the highest efficacy and not necessarily the one with the least cost. Thus Strategy 3 (OCM plus repeat OCM) has the highest efficacy and was used to determine ICER of other strategies.

Table 2: Differences in outcome between four H. pylori eradication regimen strategy

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (N)</th>
<th>Efficacy (%)</th>
<th>DURE</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>OAM</td>
<td>100.00</td>
<td>80</td>
<td>1.02</td>
<td>0.25</td>
</tr>
<tr>
<td>OCM</td>
<td>150.00</td>
<td>90</td>
<td>1.50</td>
<td>0.50</td>
</tr>
<tr>
<td>OAM-OCM</td>
<td>200.00</td>
<td>95</td>
<td>1.00</td>
<td>0.50</td>
</tr>
<tr>
<td>OCM-OCM</td>
<td>250.00</td>
<td>98</td>
<td>0.50</td>
<td>0.50</td>
</tr>
</tbody>
</table>

OAM = omeprazole, amoxicillin, and metronidazole  
OCM = omeprazole, clarithromycin, metronidazole

Table 2 includes the differences in cost and outcome between four H. pylori eradication strategies. As shown in Table 2, it will take 84 years for the cost of future relapse treatment with ranitidine to equal the extra cost of achieving a 1% increase in eradication rate with Strategy 3 (OCM plus repeat OCM) in relation to Strategy 4 (OAM plus repeat OCM). Strategy 2 (OAM) comes next after Strategy 3 with 19 years. The least is Strategy 1 (OCM) with 4 years.

One way and multi-way sensitivity analysis was conducted to test the CEA results to parameters alteration (Table 3). Varying the efficacy of OCM, Strategy 3 had the longest time for future relapse treatment cost to equal its ICER. The same applies when the ICER was estimated with range of efficacy of OAM and re-treatment with OCM. Using minimum or maximum cost of medications in the different strategies did not alter CEA result as Strategy 3 still had the longest time for future relapse treatment cost to equal its ICER.
The use of omeprazole, amoxicillin, and metronidazole in eradication of H. pylori in patients with duodenal ulcer and re-treating with omeprazole, clarithromycin, and metronidazole in patients that still shows dyspeptic symptoms is the most cost-effective option compared to the other 3 strategies. The major conclusions arrived in this analysis still holds even when some of the parameters used in the analysis were subjected to variation. This analysis could guide medical decision making in hospitals or could address the question of public subsidies for the purchase of medicines.

REFERENCES


