Varying efficacy of *Helicobacter pylori* eradication regimens: cost effectiveness study using a decision analysis model

A E Duggan, K Tolley, C J Hawkey, R F A Logan

Department of Public Health and Epidemiology, University of Nottingham, Nottingham NG7 2UH
A E Duggan, *research fellow in gastroenterology and epidemiology*
K Tolley, *lecturer in health economics*
R F A Logan, *professor of clinical epidemiology*
Division of Gastroenterology, University of Nottingham
C J Hawkey, *professor of gastroenterology*
Correspondence to: Dr Duggan anne.duggan@nottingham.ac.uk

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Abstract

Objective: To determine how small differences in the efficacy and cost of two antibiotic regimens to eradicate *Helicobacter pylori* can affect the overall cost effectiveness of *H pylori* eradication in duodenal ulcer disease.
Design: A decision analysis to examine the cost effectiveness of eight *H pylori* eradication strategies for duodenal ulcer disease with and without ^{13}C-urea breath testing to confirm eradication.
Main outcome measures: Cumulative direct treatment costs per 100 patients with duodenal ulcer disease who were positive for *H pylori*.
Results: In model 1 the strategy of omeprazole, clarithromycin, and metronidazole alone was the most cost effective of the four strategies assessed. The addition of the ^{13}C-urea breath test and a second course of omeprazole, clarithromycin, and metronidazole achieved the highest eradication rate (97%) but was the most expensive (£62.63 per patient). The cost of each additional effective eradication was £589.00 (incremental cost per case) when compared with the cost of treating once only with omeprazole, clarithromycin, and metronidazole; equivalent to the cost of a patient receiving ranitidine for duodenal ulcer relapse for more than 15 years. Eradication strategies of omeprazole, amoxycillin, and metronidazole were less cost effective than omeprazole, clarithromycin, and metronidazole alone. In model 2 the addition of the ^{13}C-urea breath test after treatment, and maintenance treatment, increased the cost of all the strategies and reduced the cost advantage of omeprazole, clarithromycin, and metronidazole alone.
Conclusion: Small differences in efficacy can influence the comparative cost effectiveness of strategies for eradicating *H pylori*. Of the strategies tested the most cost effective (omeprazole, clarithromycin, and metronidazole alone) was neither the least expensive (omeprazole, amoxycillin, and metronidazole alone) nor the most effective (omeprazole, clarithromycin, and metronidazole with further treatment for patients found positive for *H pylori* on ^{13}C-urea breath testing). Cost effectiveness should be an important part of choosing an eradication strategy for *H pylori*.

Introduction

The value of eradicating *Helicobacter pylori* in duodenal ulcer disease is well established,[1] and eradication rates in excess of 80% are regularly reported. Some regimens, however, have slightly higher eradication rates than others. The regimen of omeprazole, clarithromycin, and metronidazole has been reported to achieve a higher eradication rate than the regimen of omeprazole, amoxycillin, and metronidazole (91% *v* 85%).[1] We examined how these small differences in efficacy affect the comparative cost effectiveness of strategies for eradicating *H pylori*, and how the choice of management of patients in whom eradication treatment failed affected the comparative cost effectiveness of each eradication strategy.

There are currently two methods for treating patients with duodenal ulcer disease who remain positive for *H pylori* after eradication treatment: *(a)* identifying the patients in whom eradication treatment has been unsuccessful and giving those who are positive for *H pylori* maintenance treatment and *(b)* not testing the patients and treating only those with recurrent ulcers that produce symptoms.

We used decision analysis to investigate whether the greater effectiveness of eradication strategies based on clarithromycin for patients with duodenal ulcer disease associated with *H pylori* justifies the additional costs.

Methods

We used two decision analysis models to compare the cost effectiveness of two *H pylori* eradication regimens with or without a subsequent confirmatory ^{13}C-urea breath test, and a second course for patients in whom eradication was unsuccessful.

Decision analysis was based on DATA 2.6 software (Treeage Software, Williamstown, MA) and the Excel 5.0 spreadsheet (Microsoft, Seattle, WA).

Efficacy data—Table 1 shows the variables assessed in the models and the source of the estimates. Estimates for the eradication of *H pylori* with each regimen and the 95% confidence intervals were obtained by calculating the mean eradication rates of *H pylori* from published non-randomised trials up to November 1995.[1] For the omeprazole, clarithromycin, and metronidazole regimen there were 15 such trials, totalling 1125 patients, with an overall eradication rate of 91%, and for the omeprazole, amoxycillin, and metro-

Model 1

In model 1 it was assumed that patients in whom eradication treatment was unsuccessful would only have treatment for acid suppression if they had recurrent ulcers that produced symptoms, and in model 2 it was assumed that patients remaining positive for *H pylori* would need maintenance treatment for acid suppression to prevent ulcer recurrence and therefore would need a ^{13}C-urea breath test to show whether eradication of *H pylori* had been successful. Thus the decision analysis examined eight different strategies. In model 1 (fig 1) the four eradication strategies for *Helicobacter pylori* were:

- One week course of omeprazole 20 mg twice daily, amoxycillin 1 g twice daily, and metronidazole 400 mg twice daily
- One week course of omeprazole 20 mg twice daily, clarithromycin 250 mg twice daily, and metronidazole 400 mg twice daily
- Omeprazole, amoxycillin, and metronidazole followed by ^{13}C-urea breath testing of all patients after eradication treatment, and for patients remaining positive for *H pylori* further treatment with omeprazole, clarithromycin, and metronidazole
- Omeprazole, clarithromycin, and metronidazole followed by ^{13}C-urea breath testing of all patients after eradication treatment, and for patients remaining positive for *H pylori* further treatment with omeprazole, clarithromycin, and metronidazole

Model 2

The four strategies in model 2 therefore only differed from the four strategies in model 1 by the addition of the ^{13}C-urea breath test at the end of each treatment (fig 2).

nidazole regimen there were four such trials, totalling 673 patients, with an overall eradication rate of 85%.[1] Similar differences have been reported.[1 2] Estimates for the eradication of *H pylori* with the omeprazole, clarithromycin, and metronidazole strategy after initial failure with either regimen were obtained by calculating the mean eradiction rates of *H pylori* using this regimen in patients who had previously failed eradication treatment from all trials up to October 1996.

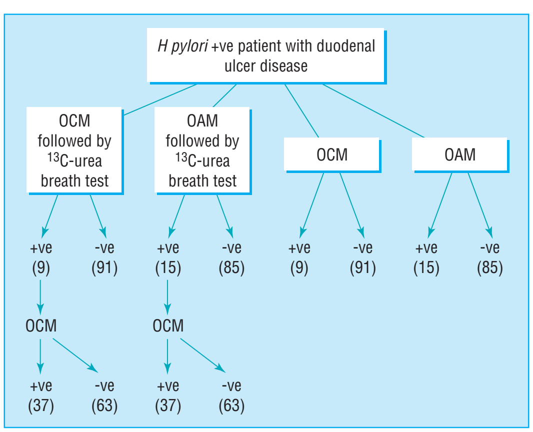

Fig 1 *H pylori* eradication strategies without confirmatory ^{13}C-urea breath testing. Bracketed figures are percentage of patients successfully treated. OCM=omeprazole, clarithromycin, and metronidazole; OAM=omeprazole, amoxycillin, and metronidazole

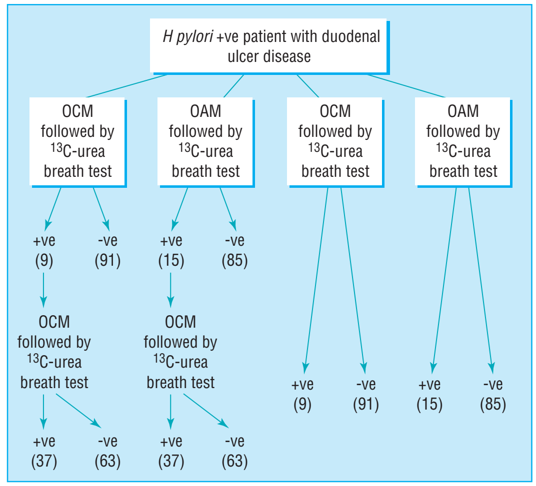

Fig 2 *H pylori* eradication strategies with confirmatory ^{13}C-urea breath testing. Bracketed figures are percentage of patients successfully treated. OCM=omeprazole, clarithromycin, and metronidazole; OAM=omeprazole, amoxycillin, and metronidazole

Cost data—As the economic analysis was conducted from the perspective of the prescriber only the direct costs of treatment were included in the analysis (table 1). The indirect costs of treatment, including the cost of consultations and the treatment of ulcer complications, were not included. The costs per patient assessment were the cost of the omeprazole, clarithromycin, and metronidazole and the omeprazole, amoxycillin, and metronidazole regimens, the cost of the ^{13}C-urea breath test, and the annual cost of maintenance and relapse treatment of duodenal ucler disease with ranitidine. Unit costs were based on the cost of NHS drug treatments from the 1996 *British National Formulary*, and the cost of the ^{13}C-urea breath test from the Bureau of Stable Isotope Analysis. Costs were valued at 1996 prices.

Table 1 Source of estimates for variables used in two models assessing cost effectiveness of eight antibiotic regimens for eradication of *Helicobacter pylori*

Variable	Base case estimate	Range	Source
Efficacy (%):			
Omeprazole, clarithromycin, and metronidazole	91	89-92	Logan, 1996
Repeat omeprazole, clarithromycin, and metronidazole after failure to eradicate *H pylori*	63	55-71	Moayyedi et al, 1995 Lamouliatte et al, 1996
Omeprazole, amoxycillin, and metronidazole	85	82-87	Logan, 1996
Cost (£):			
Omeprazole, clarithromycin, and metronidazole treatment	29.20	20-40	*British National Formulary*, 1996
Omeprazole, amoxycillin, and metronidazole treatment	20.20	10-30	*British National Formulary*, 1996
^{13}C-urea breath test	30.80	20-40	Bureau of Stable Isotope Analysis, 1996
Relapse treatment with ranitidine 150 mg twice daily (two prescriptions per year)	55.60	13.88-70.90	*British National Formulary*, 1996
Maintenance treatment of duodenal ulcer disease with ranitidine 150 mg daily (per year)	167.28	83.72-259.35	*British National Formulary*, 1996
Relapse treatment with omeprazole 20 mg daily (two prescriptions per year)	70.90		*British National Formulary*, 1996
Maintenance treatment of duodenal ulcer disease with omeprazole 10 mg daily (per year)	259.35		*British National Formulary*, 1996
Relapse treatment with cimetidine 400 mg twice daily (two prescriptions per year)	13.88		*British National Formulary*, 1996
Maintenance treatment with cimetidine 400 mg daily (per year)	83.72		*British National Formulary*, 1996
Duration of relapse treatment (weeks/year)	5.2	-	Sonnenberg, 1989

Table 2 Model 1: differences in outcome between four antibiotic strategies for eradication of *Helicobacter pylori*

Strategy	Cost (£)	% Eradication of *H pylori*	Cost of successful eradication (£)	Incremental cost of strategy 4 to strategies 1, 2, or 3 (£)*	Time (years) for future relapse treatment costs to equal incremental cost of strategy 4†	
					Not discounted	Discounted‡
1						
OAM	20.20	85	23.76	363.58	6.5	7.9
2						
OCM	29.20	91	32.08	589.59	10.6	15.7
3						
OAM+UBT+OCM	55.38	94	58.6 3	326.57	5.9	6.9
4						
OCM+UBT+OCM	62.63	97	64.78	Base	Base	Base

OAM=omeprazole, amoxycillin, and metronidazole; OCM=omeprazole, clarithromycin, and metronidazole; UBT=^{13}C-urea breath test.
*Additional cost of obtaining 1% increase in eradication rate.
†Incremental cost of strategy 4 divided by annual cost (£55.60) of relapse treatment.
‡Future costs incurred after first year of eradication treatment discounted at 6% per year.

Table 3 Model 2: differences in outcome between four antibiotic strategies for eradication of *Helicobacter pylori* with confirmatory ^{13}C-urea breath testing

Strategy	Cost (£)	% Eradication of *H pylori*	Cost of successful eradication (£)	Incremental cost of strategy 4 to strategies 1, 2, or 3 (£)*	Time (years) for future relapse treatment costs to equal incremental cost of strategy 4†	
					Not discounted	Discounted‡
1						
OAM+UBT	50.68	85	59.62	129.56	0.8	0.8
2						
OCM+UBT	60.37	91	66.34	95.76	0.6	0.6
3						
OAM+UBT+OCM+UBT	59.74	94	63.25	272.97	1.6	1.7
4						
OCM+UBT+OCM+UBT	65.80	97	68.06	Base	Base	Base

OAM=omeprazole, amoxycillin, and metronidazole; OCM=omeprazole, clarithromycin, and metronidazole; UBT=^{13}C-urea breath test.
*Additional cost of obtaining 1% increase in eradication rate.
†Incremental cost of strategy 4 divided by annual cost (£55.60) of relapse treatment.
‡Future costs incurred after first year of eradication treatment discounted at 6% per year.

Cost effectiveness analysis

We assumed that each of the eight strategies treated a hypothetical group of 100 patients with duodenal ulcer disease who were positive for *H pylori.* The decision models were constructed to estimate the proportion of patients expected to become negative for *H pylori* with each strategy, and the costs incurred. Costs and eradication rates are rounded to the nearest whole integer (figs 1 and 2 and tables 2 and 3) The cost for each successful eradication treatment of *H pylori* was calculated by dividing the total cost a strategy would incur treating 100 patients divided by the number of patients successfully treated. In each model we calculated the incremental cost of the strategy with the highest effectiveness. This was calculated as the difference between the total costs of treating 100 patients with the most effective eradication strategy compared with another strategy and dividing this total by the difference between their eradication rates. This incremental cost therefore represented the additional cost incurred for every patient that only the more effective strategy successfully treated.

The per patient cost was compared with the annual cost of treating a patient with duodenal ulcer disease remaining positive for *H pylori.* In model 1 it was assumed that patients remaining positive for *H pylori* would be treated for recurrent ulcers that produced symptoms. Therefore, the incremental cost of the most effective strategy was compared with the future cost of treatment for the symptoms of ulcer relapse with ranitidine 150 mg twice daily for 5.2 weeks per year (two prescriptions). In model 2 a ^{13}C-urea breath test was performed at the end of each strategy to identify patients still positive for *H pylori.* In this model the incremental cost of the most effective strategy was compared with the expected costs of maintenance treatment with ranitidine 150 mg daily. The unit of comparison for assessing cost effectiveness was the number of years it would take for the cumulative future cost of treating a patient with relapse, or maintenance treatment, to equal the incremental direct cost of the more effective eradication strategy. The costs of maintenance treatment for duodenal ulcer disease, and treatment for relapse of ulcers incurred after the first year, were discounted at 6% per annum to reflect the lower present value of future costs.[3] Costs were also calculated without discounting.

Sensitivity analysis

One way sensitivity analysis was performed varying the efficacy and cost estimates to identify the most important variables affecting the cost effectiveness of the strategies. Sensitivity analysis of the efficacy of the regimen for eradicating *H pylori* was conducted with 95% confidence intervals from the randomised trials of the regimens. Table 1 shows the ranges. Due to the limited and diverging data available from previous clinical trials the range of efficacy for the omeprazole, clarithromycin, and metronidazole regimen is wide for patients who remained positive for *H pylori.*

The costs of the regimens of omeprazole, clarithromycin, and metronidazole and omeprazole, amoxycillin, and metronidazole, and for the ^{13}C-urea breath test were varied by around £10 above and below the base case estimate to reflect variability in the unit price of these items. The cost of a proton pump inhibitor based treatment for maintenance and relapse treatment was also examined. Costs were based on omeprazole 10 mg daily for the maintenance treatment of duodenal ulcer disease, and omeprazole 20 mg daily for 5.2 weeks for recurrent ulcers. Two way sensitivity analysis was used to examine the effect of combinations of efficacy and cost most and least favourable to the omeprazole, clarithromycin, and metronidazole regimen.

Results

Base case analysis

Model 1 assessed the strategies without a confirmatory ^{13}C-urea breath test (table 2). The strategy of omeprazole, clarithromycin, and metronidazole followed by a further course for patients still positive for *H pylori* is the most effective strategy (97%); it is also the most expensive (£62.63 per patient treated and £64.78 per successful eradication treatment). Compared with the cost of omeprazole, clarithromycin, and metronidazole alone each additional 1% increase in eradication rate this strategy achieves costs £589.00. The strategy results in *H pylori* eradication in six more patients per 100 than omeprazole, clarithromycin, and metronidazole alone. However, the time taken for the extra costs of treating recurrent ulcers with ranitidine (150 mg twice daily for 5.2 weeks per year) in these six patients to equal these higher direct costs is 15 years (10 years if not discounted). Comparing the strategy of once only omeprazole, amoxycillin, and metronidazole with the strategy of omeprazole, clarithromycin, and metronidazole followed by ^{13}C-urea breath testing and if necessary repeat antibiotics, the costs of ranitidine based treatment for recurrent ulcers in the expected additional 12% of patients with unsuccessful *H pylori* eradication takes 8 years to equal the extra initial costs of the two stage omeprazole, clarithromycin, and metronidazole strategy. Similarly for the strategy using the cheaper omeprazole, amoxycillin, and metronidazole as the first line treatment followed by ^{13}C-urea breath testing, the direct incremental costs of omeprazole, clarithromycin, and metronidazole followed by ^{13}C-urea breath testing are equalled after 7 years (6 years not discounted).

In model 2 the use of a ^{13}C-urea breath test after treatment to confirm eradication of *H pylori* and identify eradication failures increased the costs of all strategies particularly once only omeprazole, amoxycillin, and metronidazole and once only omeprazole, clarithromycin, and metronidazole, which were the least expensive in model 1(table 3). A two stage strategy of omeprazole, clarithromycin, and metronidazole on both occasions still had the highest expected cost per successful eradication of *H pylori*. However, the incremental cost per eradication using this strategy is now less than £300 compared with the other strategies (table 3). In this model the direct initial cost advantage of a less effective strategy is short term only. The incremental direct costs of the most effective but also most expensive strategy of omeprazole, clarithromycin, and metronidazole followed by ^{13}C-urea breath testing, with further treatment and ^{13}C-urea breath testing for patients remaining positive for *H pylori*, are equalled in less than a year by the costs of maintenance treatment for ulcers for the once only omeprazole, amoxycillin, and metronidazole and once only omeprazole, clarithromycin, and metronidazole strategies, and after less than 2 years for omeprazole, amoxycillin, and metronidazole followed by ^{13}C-urea breath testing followed by omeprazole, clarithromycin, and metronidazole and further ^{13}C-urea breath testing.

Sensitivity analysis

The sensitivity of the base case estimates was tested varying the efficacy of the eradication regimens within the range shown in table 1 (table 4). In model 1, assuming a lower efficacy of 89% for the regimen of omeprazole, clarithromycin, and metronidazole initially, the expected overall eradication rate of strategies using this regimen as both first and second line treatment was reduced to 96%. The reduced efficacy of omeprazole, clarithromycin, and metronidazole most improved the comparative cost effectiveness of a two

Table 4 Sensitivity analysis of models 1 and 2 assessing cost effectiveness of eight antibiotic strategies for eradication of *Helicobacter pylori*

		No of years for future treatment costs to exceed incremental direct costs of strategy 4 (discounted)					
		Model 1			Model 2		
Variables and range	Base case estimate	Once only OAM	Once only OCM	OAM+OCM	Once only OAM	Once only OCM	OAM+OCM
Base case estimate		7.9	15.7	6.9	0.8	0.6	1.7
OCM efficacy (%):	91						
89		8.6	11.6	11.8	0.8	0.8	2.8
92		7.6	19.3	5.8	0.6	0.3	1.5
OCM efficacy after eradication failure (%):	63						
55		8.6	20.0	5.5	0.8	0.7	1.4
71		7.4	13.1	9.5	0.7	0.5	2.2
OAM efficacy (%):	85						
82		6.0	15.7	2.8	0.6	0.6	0.2
87		10.2	15.7	7.1	0.9	0.6	0.5
OCM cost per patient (£):	29.20						
20		5.7	15.1	0.0	0.2	0.5	0.0
40		11.0	16.5	27.5	1.4	0.7	4.8
OAM cost per patient (£):	20.20						
10		10.6	15.7	27.6	1.3	0.6	4.8
30		5.8	15.7	0.0	0.3	0.6	0.0
UBT cost: per patient (£):	30.80						
20		5.6	9.0	7.3	0.7	0.5	1.9
40		10.4	24.9	7.3	0.8	0.7	1.6
Efficacy and costs to OCM:							
Most favourable*		3.3	>50	0.0	0.0	0.5	0.0
Least favourable†		29.9	15.4	>50	3.1	0.9	>50
Treatment cost of recurrent ulcers per year (£):	55.60						
13.88		>50	>50	>50			
70.90		5.9	10.9	5.2			
Maintenance treatment cost per year (£):	167.28						
83.72					1.6	1.2	3.5
259.35					0.5	0.4	1.1

OAM=omeprazole, amoxycillin, and metronidazole; OCM=omeprazole, clarithromycin, and metronidazole.
*OCM efficacy 92%, OCM efficacy after eradication failure 71%, OAM efficacy 82%, OCM £20 per patient, OAM £30 per patient.
†OCM efficacy 89%, OCM efficacy after eradication failure 55%, OAM efficacy 85%, OCM £40 per patient, OAM £10 per patient.

stage strategy with omeprazole, amoxycillin, and metronidazole instead of omeprazole, clarithromycin, and metronidazole as first line treatment. This strategy was comparable in cost effectiveness with the strategy of once only omeprazole, clarithromycin, and metronidazole. For omeprazole, amoxycillin, and metronidazole and omeprazole, clarithromycin, and metronidazole a total of more than 13 years of treatment for relapses would be required to exceed the direct incremental costs of the two stage omeprazole, clarithromycin, metronidazole strategy (10 years not discounted), and for the omeprazole, clarithromycin, and metronidazole strategy more than 11 years (9 years not discounted) (table 4).

In model 1 assuming an efficacy of only 55% for omeprazole, clarithromycin, and metronidazole when given as second line treatment had no effect on the comparative cost effectiveness of the alternative strategies. In only two situations (table 4) were omeprazole, amoxycillin, and metronidazole based strategies more cost effective than omeprazole, clarithromycin, and metronidazole alone. Firstly, increasing the cost of the omeprazole, clarithromycin, and metronidazole regimen to £40.00 made the omeprazole, amoxycillin, and metronidazole followed by omeprazole, clarithromycin, and metronidazole strategy more cost effective than omeprazole, clarithromycin, and metronidazole alone. The two stage strategy with first line treatment with omeprazole, amoxycillin, and metronidazole had a cost advantage compared with the two stage strategy of omeprazole, clarithromycin, and metronidazole for over 27 years of treatment for relapses (14 years not discounted). Secondly, assuming the least favourable efficacy (89%) and costs (£40) for omeprazole, clarithromycin, and metronidazole resulted in both omeprazole, amoxycillin, and metronidazole based strategies being more cost effective. The strategy of once only omeprazole, amoxycillin, and metronidazole achieved a cost advantage for 30 years of treatment of relapses (14 years not discounted) and the two stage strategy of omeprazole, amoxycillin, and metronidazole for over 50 years.

Relative cost effectiveness was not sensitive to any of the other ranges used, to the other efficacy variables, or to the cost of the ^{13}C-urea breath test. In each case a strategy of once only omeprazole, clarithromycin, and metronidazole had the best outcome. The number of years, however, for the cost of treatment for relapses for the additional patients positive for *H pylori* to exceed the incremental costs of the two stage strategy of omeprazole, clarithromycin, and metronidazole was sensitive to the annual cost of treatment for relapses. If an annual cost of treatment for recurrent ulcers of £70.90 per patient is incurred for a treatment based on omeprazole (expected relapse of 5.2 weeks per annum of full dose treatment) the incremental direct costs of a two stage strategy of omeprazole, clarithromycin, and metronidazole are equalled in just over 10 years (8.3 years not discounted). For the other two strategies only about 6 years are required.

In model 2 using the confirmatory ^{13}C-urea breath test no single variable in the sensitivity analysis substantially changed the comparative dominance of the two stage strategy of omeprazole, clarithromycin, and metronidazole. Only one combination of variables—that representing the least favourable efficacy and cost scenario for the regimen of omeprazole, clarithromycin, and metronidazole (89%, £40.00 per patient)—greatly altered the difference between the cost effectiveness of the strategies. This produced an estimate of over 50 years for the cost of a strategy of omeprazole, amoxycillin, and metronidazole then omeprazole, clarithromycin, and metronidazole and maintenance treatment to exceed the incremental costs of a strategy of omeprazole, clarithromycin, and metronidazole then omeprazole, clarithromycin, and metronidazole (17.8 years not discounted). Increasing the cost of maintenance treatment for ulcers improved the comparative cost effectiveness in favour of the more effective eradication strategies. The initial cost savings associated with the strategy of omeprazole, amoxycillin, and metronidazole then omeprazole, clarithromycin, and metronidazole comparative to the two stage strategy of omeprazole, clarithromycin, and metronidazole would be lost within a short time (1.5 years) and would make it difficult to justify its preference.

Discussion

It is now well established that eradication treatment for *H pylori* is more cost effective than either treatment for recurrent ulcers or maintenance treatment for duodenal ulcer disease.[4 5] However, the comparative cost effectiveness of various regimens for eradicating *H pylori* is not clear. A clinical trial to evaluate this would be difficult as it requires a large number of patients and long and detailed follow up. Decision analysis models therefore provide useful information and guidance in situations where trial data is unavailable or difficult to obtain.

The variables used in this model are consistent with the findings of randomised comparisons of regimens of omeprazole, clarithromycin, and metronidazole and omeprazole, amoxycillin, and metronidazole, and of another review of trials of *H pylori* eradication.[1 2] If anything these studies have found slightly larger differences in the efficacy of these two regimens than we have applied in our models. The magnitude of the difference in cost effectiveness of the regimens we have tested may therefore be greater.

Using the variables chosen, we have shown that from the prescriber's perspective even small differences in efficacy of these highly effective antibiotic regimens result in large differences in the direct cost of treating patients with duodenal ulcer disease who are positive for *H pylori*. In this analysis choosing *H pylori* eradication strategies on the basis of cost or efficacy alone did not identify the most cost effective strategy. If patients who fail eradication treatment are only treated for symptomatic relapses, once only treatment with omeprazole, clarithromycin, and metronidazole was the most cost effective approach to *H pylori* eradication despite being more expensive than omeprazole, amoxycillin, and metronidazole, and less effective than the two stage strategy of omeprazole, clarithromycin, and metronidazole. This is because the incremental costs of the most effective strategy of two stage omeprazole, clarithromycin, and metronidazole takes at least 15 years to be equalled (10 years if not discounted).

This analysis also shows how strongly subsequent management of patients remaining positive for *H pylori* influences the comparative cost effectiveness of eradication strategies. Aiming for higher eradication rates and thereby incurring higher initial costs becomes more cost effective if patients who ultimately fail eradication treatment receive maintenance treatment. However, as model 2 shows, testing all patients at the end of treatment with the ^{13}C-urea breath test greatly increases the direct costs of eradication treatment. Using highly effective regimens means testing a large number of patients to identify a few who are positive for *H pylori*. The value of confirming whether eradication of *H pylori* has been successful is even more questionable if patients positive for *H pylori* are only treated for recurrent ulcers that produce symptoms.

Our results were sensitive to the cost of relapse treatment (model 1). The effects of treatment with a proton pump inhibitor or the less expensive cimetidine were considered in the sensitivity analysis. Using the more costly proton pump inhibitor for relapse treatment would substantially decrease the expected cost advantage of lower eradication rates with once only omeprazole, clarithromycin, and metronidazole over the more effective rates expected with the strategy of two stage omeprazole, clarithromycin, and metronidazole. However, the time taken for the costs associated with unsuccessful eradication to accrue is important. In older patients it may exceed life expectancy and therefore make the treatment of relapses with proton pump inhibitors still more cost effective than the initial higher outlay of more effective eradication strategies.

A number of caveats apply to any economic evaluation. This study is limited to analysing the direct costs to the health service. A cost has not been included explicitly for visits to the doctor which would occur in conjunction with each ^{13}C-urea breath test. The effect, however, of allowing a sum of £10.00 for each visit can be seen in the sensitivity analysis (table 4). The clinical decision between choosing costly but highly effective initial eradication strategies or higher ongoing costs of maintenance treatment for ulcers or treatment of relapses will depend on the true cost of treating continuing duodenal ulcer disease, which will be higher than drug costs alone.[6] Ongoing costs also depend on the life expectancy and comorbidity of the patient and the incidence and costs of complications in ulcers that recur.[6–10] Quality of life and other health outcomes associated with the eradication of *H pylori* or continued duodenal ulcer disease also need to be considered in any clinical decision. The results of a number of clinical studies are available providing information on these aspects of management.[8 10] Although most data on the efficacy of various eradication strategies are based on studies in secondary care similar results have been obtained from studies in primary care.[11]

To reflect how clinicians make decisions about drug treatment this study compared eradication strategies directly. Some authors have suggested an alternate strategy of ordering strategies according to efficacy and assessing the incremental cost effectiveness of each strategy compared with the next most effective strategy after excluding dominated strategies—that is, those with lower efficacy or higher costs than another strategy.[12] This assumes that doctors or purchasers change treatments according to their willingness or ability to pay for the additional efficacy. While this is appropriate for consideration of the theoretical cost effectiveness of new drug treatments it does not sufficiently reflect the way doctors make decisions about switching from one drug treatment to another. For this reason in this economic analysis we compared each alternative strategy against the strategy with the greatest efficacy. Reanalysing our data to show the incremental cost effectiveness of each strategy compared with the next most effective strategy did not substantially alter the results.

Key messages

- It is unlikely that randomised controlled trials to examine the effect of small differences in efficacy and cost between eradication regimens will ever be performed because of the large numbers of patients required
- Decision analysis models show that relatively small differences in efficacy and cost between several strategies for eradication of *H pylori* in patients with duodenal ulcer disease lead to large differences in their relative cost effectiveness
- The most cost effective strategy was neither the least expensive nor the most effective for eradication of *H pylori*
- For uncomplicated duodenal ulcer disease performing a ^{13}C-urea breath test to identify patients failing eradication treatment is not cost effective if patients only receive acid suppression treatment for relapses that produce symptoms
- Performing a ^{13}C-urea breath test to identify patients failing eradication treatment may only be cost effective in high risk patients

Conclusion

Our analysis shows the value of decision analysis in situations where the results of clinical studies are not available to assess the implications of treatment choice. In particular the analysis shows the great difference in overall cost of broadly similar strategies for the eradication of *H pylori* in patients with duodenal ulcer disease. At a community level the effect of these differences on the overall cost of treating duodenal ulcer disease should be even greater.

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Commentary: *Helicobacter pylori* eradication in primary care

Brendan C Delaney, F D Richard Hobbs

Department of General Practice, Medical School, University of Birmingham, Edgbaston, Birmingham B15 2TT

Brendan C Delaney, *senior lecturer*

F D Richard Hobbs, *professor*

Correspondence to: Dr Delaney b.c.delaney@bham.ac.uk

Decision analysis is a useful aid to judgment particularly where a balance between the relative costs and effectiveness of different treatments is sought.[1] Although eradication treatment for *Helicobacter pylori* has been shown to prevent most recurrent peptic ulcers, multiple treatment with a proton pump inhibitor and at least two types of antibiotic is required to achieve good eradication rates.[2] As there are a number of eradication regimens, of differing costs, there is a need for a rational basis from which to make a choice. The success of this eradication treatment may be reliably confirmed by a breath test, using urea labelled with carbon-13 or carbon-14. The urea breath test can be performed as an outpatient procedure or in primary care using a test kit (Bureau of Stable Isotope Analysis, Brentford).

The comparative cost effectiveness of eradication treatment depends on the costs of failure. Duggan et al's paper considers two different strategies for dealing with the costs of failure: waiting for recrudescence of symptoms and prescribing ranitidine 150 mg twice daily to heal recurrent ulcers; or breath testing all patients to confirm eradication, and prescribing ranitidine 150 mg once daily as maintenance treatment to prevent further ulcers in patients in whom treatment has failed.

The validity of a decision analysis depends on the initial assumptions and strategies compared. Despite differing absolute costs the domination of one treatment by another and the factors that might overturn this in a sensitivity analysis should be applicable to particular local circumstances. For example, despite Duggan et al's data showing that the time taken to recoup the additional costs of eradication treatment is a factor of fivefold longer than that previously estimated by Briggs et al, using different cost assumptions,[3] eradication is still the most cost effective management of peptic ulcer disease.

Duggan et al's analysis indicates that more costly, but more effective, eradication regimens are justified if the costs of failed treatment are high. It is unlikely that general practitioners would want to breath test every patient treated especially as symptom recurrence has been shown to be predictive of relapse.[4] Breath testing, however, is useful in discriminating between patients who have recurrent symptoms due to failed eradication treatment and those, possibly as many as 30%,[5] who have coexisting reflux or non-ulcer dyspepsia.

If usual practice is to treat recurrent dyspeptic symptoms with intermittent acid suppression alone, an inexpensive regimen of proton pump inhibitor, amoxycillin, and metronidazole would be the most cost effective eradication treatment. More expensive management strategies incorporating further investigation or maintenance treatment with a proton pump inhibitor lead to eradication regimens based on clarithromycin being more cost effective. Knowing this should not only help doctors to decide on the most appropriate regimen, but also highlights the important consequences of different management strategies for persistent symptoms. In practice, however, many other factors—for example the potential for metronidazole resistance, side effects, and possible reactions—will also play a role in this decision.

Although prescribing for dyspepsia is now the largest single area of cost for primary care (£500 million per year in the United Kingdom in 1996) the principal cause of this has been proton pump inhibitors prescribed for oesophageal reflux or non-ulcer dyspepsia. Duggan et al cannot address the problems of how best to manage the newly presenting patient with dyspepsia or how to treat non-ulcer dyspepsia as their analysis is confined to peptic ulcer disease. These issues will have to await the results of trials currently in progress, and further modelling studies.

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Endpiece

Alternative definitions

Barometer: An ingenious device which indicates the kind of weather we are having.

Ambrose Bierce, *The Cynic's Word Book* (1906), subsequently titled *The Devil's Dictionary*