Cost effectiveness of screening for and eradication of *Helicobacter pylori* in management of dyspeptic patients under 45 years of age

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Abstract

Objective—To assess the cost effectiveness of screening for and eradicating *Helicobacter pylori* in patients under 45 years of age presenting with dyspepsia.

Design—A decision analytic model composed of a decision tree to represent the epidemiology of dyspepsia and a Markov process to model the outcomes of treatment.

Patients—Patients under the age of 45 years presenting to their general practitioner with (peptic type) dyspepsia.

Interventions—Conventional empirical treatment with healing and maintenance doses of cimetidine v eradication treatment solely in patients with confirmed peptic ulcer; and conventional empirical treatment for all dyspeptic patients compared with the use of a serology test to identify patients with *H pylori*, who then receive endoscopy to investigate the presence of peptic ulcer disease and, when disease is found, are given eradication treatment with a breath test to confirm successful eradication.

Main outcome measures—Expected cumulative costs over a period of 10 years. The proportion of time patients spend without a recurrent ulcer.

Results—After receiving eradication treatment, patients with confirmed ulcer spend an average of 99% of their time free from recurrent ulcer disease compared with 95% after treatment with cimetidine. Eradication treatment costs less than that with cimetidine. When the initial cost of identifying appropriate patients to receive eradication treatment is added to the analysis, however, these cost savings take almost eight years to accrue.

Conclusions—Enthusiasm for introducing testing for and eradication of *H pylori* for dyspeptic patients in general practice should be tempered by an awareness that cost savings may take many years to realise.

Introduction

Several recent publications have reported the major benefits associated with eradicating *Helicobacter pylori* infection in patients with confirmed ulcer, both in terms of improved health outcomes for patients and substantial cost savings to the health service.¹⁻⁵

Endoscopy is not usually indicated in young dyspeptic patients who, given the safety and efficacy of antisecretory drugs, are often managed empirically with one or more healing courses of H₂-receptor antagonists, followed by either a daily maintenance dose or empirical treatment as symptoms recur. Hence, although patients over the age of 45 years are often referred for endoscopy (because of the higher risk of carcinoma⁶⁻⁹), many patients presenting with dyspepsia in general practice are not investigated. A major drawback to the current management of dyspepsia is the cost of empirical treatment with antisecretory medication, which is now one

of the most expensive cost categories in NHS drug expenditure. *H pylori* infection is the principal cause of peptic ulcer,^{10,11} and eradication of the infection prevents and effectively cures peptic ulcer disease. A recent consensus conference of the National Institutes of Health in the United States concluded that only those patients with ulcer and *H pylori* infection should be offered eradication treatment as there was no proved benefit associated with *H pylori* eradication in dyspeptic patients without ulcer.¹² Preliminary assessments would suggest considerable cost savings could be achieved by using this strategy.^{3,4,9,13} Clinical policy, however, should consider how the potential beneficiaries of treatment for *H pylori* eradication can be identified in a cost effective manner from among an estimated 40% of patients presenting with dyspepsia each year who are under the age of 45 years.⁷

We present the results of two cost effectiveness analyses from a health service perspective. We used a decision analytic model to characterise the identification and treatment of peptic ulcer and incorporated data available in the published literature. The first analysis examined the cost and effectiveness of eradication treatment versus conventional antisecretory treatment in patients with confirmed peptic ulcer disease. The second analysis considered the cost and effectiveness of these strategies but included the process of identifying ulcer patients for eradication treatment.

Methods

The decision analytic model was made up of two parts. The first part was a Markov model to characterise the treatment of patients with peptic ulcer who were positive for *H pylori* and to evaluate the cost effectiveness of conventional empirical antisecretory treatment versus eradication treatment in those patients. The second part augmented the Markov model to assess the overall cost effectiveness of identifying patients with *H pylori* and peptic ulcer and of providing eradication treatment compared with conventional empirical treatment. Modelling was undertaken by using DATAV2.5.¹⁴ The model was subject to quality control by replicating the results with Quattro Pro v6.0.¹⁵ Table 1 gives a full list of all parameters used in the model, their base case estimates, and the source of those estimates.

MODELLING THE TREATMENT OF PEPTIC ULCER PATIENTS

A Markov model was used to represent the costs and outcomes associated with the empirical treatment of recurrent ulcer with cimetidine versus a standard triple eradication treatment based on bismuth. Cimetidine was chosen as the cheapest antisecretory agent. The methods for using Markov models in health services research are well documented.^{16,17} In brief, Markov models entail splitting a patient's possible prognoses into a number of states. The probabilities defining transition between each of these states are specified over a specific time frame such as a month or a year, and the

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Table 1—Base case estimates and source of estimates for all model parameters

Model parameter	Base case estimate	Source
Four week rates of healing of ulcer with cimetidine healing dose	80%	Katz and Hollander ¹⁸
Four week rate of recurrence of ulcer from state of remission	6%	Pym <i>et al</i> ²⁹
Four week rate of recurrence of ulcer with maintenance cimetidine	3%	Pym <i>et al</i> ²⁹
Yearly rate of reinfection with <i>Helicobacter pylori</i>	1%	Campbell, Bell <i>et al</i> ³⁰
Success of eradication treatment (first attempt)	80%	Tytgat ³¹
Success of eradication treatment (after two attempts)	94%	Table 2
Prevalence of <i>H pylori</i> among dyspeptic patients (<45 years)	40%	See text
Prevalence of peptic ulcer disease among patients positive for <i>H pylori</i>	25%	Patel <i>et al</i> ²⁶
Prevalence of peptic ulcer disease among patients negative for <i>H pylori</i>	3%	Patel <i>et al</i> ²⁶
Sensitivity of the serology test (for detecting <i>H pylori</i>)	77%	Duggan <i>et al</i> ³²
Specificity of the serology test	89%	Duggan <i>et al</i> ³²
Sensitivity of endoscopy (for detecting peptic ulcer disease)	100%	See text
Specificity of endoscopy	100%	See text
Cost of consultation with general practitioner	£7.92	Netten ³³
Cost of outpatient attendance	£38.66	Chartered Institute ³⁴
Cost of ¹³ C-urea breath test	£30.80	BSIA*
Cost of serology test	£12.77	Cortecs†
Cost of endoscopy	£76.38	British Society of Gastroenterology ³⁵
Cost of formulation of eradication treatment	£38.49	BNF‡ ³⁶ table 2
Cost of course of eradication treatment (average)	£131.12	Table 2
Cost of four week healing course of cimetidine	£21.00	BNF‡ ³⁶
Cost of four week maintenance course cimetidine	£10.00	BNF‡ ³⁶
Annual discount rate	6%	Treasury ²⁴

*Bureau of Stable Isotope Analysis (BSIA), Brentford, 1995.

†Cortecs Diagnostics, Clwyd, 1995.

‡British National Formulary.

model is then run over a large number of periods to see how a patient would move between states. The probabilities can be redefined for each treatment being evaluated, and the costs and effects of treatments can be estimated according to the time spent in each state. Figure 1 presents the structure of the Markov model, with ovals representing the possible disease states and arrows indicating possible transitions between those states. A four week time frame was taken for the model: equivalent to the standard duration of a single treatment with H₂-receptor antagonists.

The model was structured with the following assumptions. Under conventional treatment we assumed that patients presenting with peptic type dyspepsia are given a healing course of cimetidine

(800 mg a day for four weeks). If after this course the ulcer has not healed (that is, if the symptoms have not resolved), a second healing course is prescribed. Healing rates at four weeks for cimetidine are about 80%¹⁸ with almost every ulcer having healed after 12 weeks of treatment.¹⁹ For the purposes of this model we assumed that a third healing course would heal all ulcers which persist beyond eight weeks. Once their ulcers heal most patients will enter a "remission" state when they have no ulcer and receive no medication. Each month there is a chance that patients will experience a recurrence of their ulcer, in which case they begin with the first course of ulcer healing drugs once more. Those patients whose ulcers persist beyond eight weeks after the first occurrence or four weeks after the first recurrence and all those patients who experience a second recurrence were assumed to receive long term maintenance treatment once their ulcers had healed. This treatment entails a maintenance dose of cimetidine (about half the healing dose) taken each day for the duration of the model. Ulcers can recur while patients are on maintenance treatment, in which case patients receive healing doses again followed by maintenance doses once the ulcer has healed.

The Markov model presented in figure 1 also shows a state of "cure" for those patients who have received successful eradication treatment. Success of eradication treatment is determined by using a carbon-13 (¹³C) labelled urea breath test conducted at hospital. Although no test for *H pylori* infection is perfect, this test has been shown to produce consistently accurate results,^{20 21} and for the sake of simplicity in this model the ¹³C-urea breath test is assumed to have a sensitivity and specificity of 100%. When eradication of *H pylori* is unsuccessful, patients receive a second course of eradication treatment. This second course is assumed to be less effective than the first because of increased antimicrobial resistance. Those patients who become reinfected with *H pylori* are assumed to experience a recurrence of their ulcer and to receive conventional empirical treatment with H₂-receptor antagonists.

The Markov model was used to compare patients with peptic ulcer treated conventionally (who start with the first healing dose state of the model) with ulcer patients receiving eradication treatment (who begin the model in the "cure" state if *H pylori* was successfully eradicated, otherwise they start with the first healing dose of cimetidine as with conventional treatment). The success rate of eradication treatment depends on the regimen used. A standard triple treatment formulation based on bismuth was used in this model; dosages, costs, and success rates are presented in table 2. The Markov model was run for 10 years to show how the costs of conventional versus eradication treatment accumulate over time for patients with peptic ulcer disease.

Fig 1—Markov model characterising the empirical treatment of dyspepsia with cimetidine. A state of cure is also shown for successful eradication treatment. Patients who receive unsuccessful *Helicobacter pylori* eradication treatment or who become reinfected are treated conventionally

CLASSIFYING DYSPEPIC PATIENTS

To extend the cost effectiveness analysis to a strategy of combined screening for and eradication of *H pylori* in patients with peptic ulcer, it is necessary to estimate the proportion of patients with the potential to benefit from such a strategy from among the dyspeptic population. Therefore, the second part of the model classified dyspeptic patients by the presence or absence of *H pylori* infection and by whether or not peptic ulcer is the underlying cause of their symptoms. Figure 2 presents these four categories of dyspepsia in the form of a probability tree. The probabilities at each of the circular "chance nodes" represent the prevalence of *H pylori* infection among patients with dyspepsia, the proportion of seropositive patients with ulcer disease, and the proportion of seronegative patients with ulcer disease.

The community based prevalence in the United Kingdom of *H pylori* in patients under 45 years of age

Table 2—Triple eradication treatment: formulation costs and effectiveness

Detail	Dose and duration	Effectiveness	Cost
Cost of triple eradication treatment			
Formulation cost:			
Tripotassium dicitratobismuthate (De Nol Tab)	1 Four times daily for 14 days		£14.70
Amoxycillin (Amoxil capsules)	500 mg Thrice daily for 14 days		£14.70
Metronidazole (Flagyl tablets)	400 mg Thrice daily for 14 days		£9.09
Total			£38.49
Additional costs:			
Checking test (¹³ C-urea breath test)			£30.80
Cost of outpatient attendance			£38.66
Total cost of triple eradication treatment			£107.95
Effectiveness of triple eradication treatment			
After one course		80%	
After retreatment		70%	
Total effectiveness after retreatment for first time failure of treatment		94%	
Total cost of eradication treatment*			£131.12

*Including retreatment and additional visit to general practitioner for first time failure of treatment.

Fig 2—Probability tree showing underlying disease of patients presenting with dyspepsia

with dyspepsia is unknown. A lower estimate, however, equivalent to the prevalence of *H pylori* in a randomly selected sample of a community based population aged under 45 years in the United Kingdom ranges between 19% and 36%²²; while in patients who have been investigated in hospital and found to have non-ulcer dyspepsia, prevalence figures range from about 40% to 58%.²³ We assumed in the base case analysis that the prevalence of *H pylori* in dyspeptic patients under 45 years of age presenting to their general practitioner was 40%, a midpoint between these two extremes. Variation in this estimate was explored in the sensitivity analysis.

To identify the appropriate patients to receive eradication treatment, all dyspeptic patients receive a serology test for *H pylori*, and those with positive results receive further investigation by endoscopy to determine whether they have peptic ulcer disease. For the sake of simplicity the results of endoscopy were assumed to be 100% sensitive and specific; this assumption was then tested in the sensitivity analysis. Under the screening and eradication strategy, some patients without *H pylori* related peptic ulcer disease will receive inappropriate eradication treatment. As their symptoms will persist, however, they will be returned to conventional empirical treatment. Hence, the difference in costs between the two management strategies for these patients is simply the additional cost of the inappropriate eradication treatment.

COSTS

Only health service costs were considered, the bulk of which comprise the drug costs of eradication treatment or cimetidine, but which also include the cost of consul-

tations with general practitioners for symptoms, entailing prescription of healing H₂-antagonists or eradication treatment, and a ¹³C-urea breath test to check the success of the eradication treatment. Patients in the "cure" or "remission" states of the model were assumed not to consume any resources. All costs were discounted at the Treasury rate of 6% a year to allow for differential timing²⁴ and were adjusted to 1995 prices when appropriate.

SYMPTOMS

Data on symptoms experienced by patients with peptic ulcer disease receiving H₂-antagonist treatment are sparse. In this model, health outcomes were measured in terms of the proportion of time patients spend without a recurrent ulcer—that is, in a state of "cure," in remission, or on maintenance cimetidine.

Results

CONVENTIONAL VERSUS ERADICATION TREATMENT FOR PEPTIC ULCER

The results of the Markov model showed that the higher initial cost of *H pylori* eradication treatment is quickly offset by the avoidance of long term cimetidine treatment, indicating that *H pylori* eradication treatment is cost saving compared with H₂-antagonist treatment, with the magnitude of these savings increasing over time. The average cost per patient of conventional treatment after 10 years was £812 compared with a total 10 year cost of £209 for those patients who initially receive eradication treatment (fig 3).

The average proportion of time spent without ulcer (and therefore without symptoms) for patients in the model was 99% for triple treatment eradication compared with 95% for conventional treatment. These figures reflect the fact that H₂-antagonists are an effective treatment for controlling symptoms of peptic ulcer but that eradication of *H pylori* infection effectively cures the condition for most patients. As the difference in effectiveness is small (and clearly in favour of eradication treatment), the subsequent analysis focuses on costs.

SCREENING AND ERADICATION STRATEGIES

Figure 2 shows that only 10% of dyspeptic patients have both *H pylori* infection and peptic ulcer. The results of comparing a screening strategy to identify these patients from among the dyspeptic population with conventional empirical cimetidine treatment are presented in figure 4. The cost of screening increases expenditure in the first year. Only as the costs associated with long term maintenance treatment accrue does the screening strategy finally result in savings, after almost eight years.

SENSITIVITY ANALYSIS

Sensitivity analysis examines the implications for the results of an evaluation of varying its parameters.²⁵ Table 3 presents the results of such an analysis in relation to the comparison of the screening and eradication strategy with conventional management. Given the focus on costs, the sensitivity analysis concentrated on the payback period for the initial investment in screening and eradication strategy—that is, the point in time at which the costs of both strategies are equal.

It is clear from table 3 that the prevalence of *H pylori* infection among dyspeptic patients is a key parameter of the model. If an upper estimate of 60% is used the payback period is seven years. A lower estimate of 20% produces a payback period of 12 years. The prevalence of ulcer among those seropositive for *H pylori* is also a key parameter, although variation in the prevalence of ulcer among dyspeptic patients negative for *H pylori* has little effect on the payback period. The cost and accuracy of

Fig 3—Ten year accumulation of costs for conventional v *Helicobacter pylori* eradication treatment for patients with confirmed infection and peptic ulcer disease

Table 3—Results of sensitivity analysis

Parameter	Base case value	Range of values*	Payback period (years)†
Prevalence of <i>Helicobacter pylori</i>	40%	20%-60%	12-7
Proportion of patients with <i>H pylori</i> and peptic ulcer	25%	20%-50%	10-5
Proportion of patients without <i>H pylori</i> but with peptic ulcer	3%	0%-10%	8-8
Cost of serology test	£12.77	£6-£24	7-9
Sensitivity of serology test	77%	60%-100%	7-9
Specificity of serology test	89%	70%-100%	9-7
Cost of formulation of eradication treatment	£38.49	£20-£60	8-8
Effectiveness of eradication treatment (after two attempts)	94%	70%-100%	10-7
Cost of endoscopy	£76.38	£50-£100	7-9
Sensitivity of endoscopy	100%	80%	8
Specificity of endoscopy	100%	80%	9
Cost of breath test	£30.80	£20-£40‡	8-8
Cost of outpatient attendance	£38.66	£30-£50	5-18
Cost of antisecretory healing dose	£21.00	£10-£35§	7-8
Cost of antisecretory maintenance dose	£10.00	60%-90%	9-7
Four week healing rate on cimetidine	80%		
Rate of recurrence of ulcer (with maintenance cimetidine treatment)	2.49%	1%-4%‡	
Ulcer recurrence rate (without treatment)	5.72%	4%-8%	

*In the absence of good quality data on likely variation in each parameter, ranges of values have been chosen arbitrarily by us to show likely importance of variation in each parameter for results of analysis.

†Payback period has been rounded to nearest whole year.

‡Parameters varied simultaneously in sensitivity analysis.

§Upper estimates refer to 20 mg healing dose/10 mg maintenance dose of proton pump inhibitor daily for four weeks; lower estimates refer to same dose of generic rather than proprietary cimetidine.

the serology test also have important effects on the payback period, as does the cost of an endoscopy, because of their effect on the cost of identifying patients for *H pylori* eradication treatment. By contrast, the accuracy of endoscopy is not an important parameter. A plausible variation in the cost of *H pylori* eradication treatment has little overall effect on the period until cost savings are apparent. Improving the effectiveness of eradication treatment to 100% will have little effect on the payback period, although this period is much more sensitive to assumptions of reduced effectiveness. Variation in the costs of a ¹³C-urea breath test and in outpatient attendance have little effect as these affect only the overall cost of eradication treatment. The recurrence rates for ulcer will affect the overall cost of conventional treatment and are therefore key parameters for this model.

The most important parameter with respect to the payback period was the cost of antisecretory medication. In the base case analysis, the proprietary price of cimetidine was used as this was thought to be the most common treatment for peptic-type dyspepsia. Increasingly, however, many general practitioners favour proton pump inhibitors over cimetidine, which have similar ulcer healing properties but which cost almost twice as much. With the price of a proton pump inhibitor as an upper estimate, the sensitivity analysis showed that if general practitioners favoured inhibitors over H₂-receptor antagonists for the treatment of peptic type dyspepsia, it would take five years for an *H pylori* screening and eradication strategy to yield cost savings. Generic H₂-receptor antagonists, however, have recently become available. With the price of generic cimetidine as the lower estimate, the sensitivity analysis suggests that when general practitioners are prescribing generic H₂-receptor antagonists the payback period for a screening and eradication strategy could be as long as 18 years.

Discussion

Other economic evaluations of the use of *H pylori* eradication treatment as an alternative to maintenance treatment with H₂-receptor antagonists have tended to

focus their analysis on the group of seropositive patients with confirmed peptic ulcer. It is clear from the results presented in figure 4, however, that this is potentially misleading. The implication of these earlier results is that the NHS could save money in the first year of treatment if general practitioners were to switch to an *H pylori* eradication programme for appropriate dyspeptic patients. In fact, if the recent proposals for screening dyspeptic patients, with endoscopy for patients whose tests yield positive results, were to be implemented^{8 26 27} it may be almost eight years before any cost savings are realised. Furthermore, the initial costs in the first year may be over £50 per patient in excess of the costs of empirical treatment with cimetidine. Clearly, such a disparity between the length of time before the NHS can expect to see cost savings as a result of a switch to an *H pylori* screening strategy could have important implications for both fundholders and purchasing authorities who try to balance their budgets on a year by year basis. Even by allowing for a reasonable level of uncertainty, it will be at least five years before cost savings are realised, although it may take as long as 18 years.

There are several problems associated with modelling the course of *H pylori* eradication treatment in the way we have presented. The underlying assumptions of the model may not reflect clinical practice. In particular, the assumption that the treatment of patients with non-ulcer dyspepsia will not change as a result of implementing a screening strategy entailing testing for *H pylori* is likely to bias the results against eradication treatment. In theory, general practitioners might interpret a negative test result as a sign that patients are unlikely to have peptic ulcer and so prescribe fewer antisecretory drugs, although in fact preliminary data suggest this does not occur.²⁸ Further research is required to assess the prescribing habits of general practitioners after the results of *H pylori* testing.

The long payback period associated with adopting a screening and eradication strategy in general practice is partly due to the low proportion of patients with both *H pylori* infection and peptic ulcer disease for whom eradication treatment is appropriate. It is also due to the fact that the screening strategy entails all patients testing positive for *H pylori* undergoing endoscopy, an investigation which would not have been undertaken under conventional management. If eradication treatment were shown to be of benefit in non-ulcer dyspepsia, then a policy of eradication in all patients with positive results could be justified, thereby avoiding the need for endoscopy. Current evidence suggests, however, that there is no proved benefit of eradicating the infection in these patients.¹² Moreover, one of the most common causes of non-ulcer dyspepsia is gastro-oesophageal reflux, which is not helped by eradication treatment but is improved by antisecretory drugs.

CONCLUSIONS

Although *H pylori* eradication treatment has been shown to be cost saving in the treatment of seropositive patients with peptic ulcer disease, considerable caution should be exercised when extrapolating such results to the screening of dyspeptic patients for *H pylori* in routine clinical practice. Cost savings will eventually accrue, but this may take some years, which contrasts with the immediate cost savings implied in the literature. The actual cost effectiveness of strategies for *H pylori* screening and eradication may depend crucially on the effect of eradication treatment on non-ulcer dyspepsia rather than for peptic ulcer where the benefits have been established.

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Fig 4—Difference in costs between conventional cimetidine treatment and strategy of identifying appropriate patients to receive *Helicobacter pylori* eradication treatment

Key messages

- Eradication treatment is cost effective for the treatment of confirmed peptic ulcer
- Patients under the age of 45 years presenting with peptic-type dyspepsia without sinister symptoms are usually managed empirically
- Only a minority of these patients will have peptic ulcer disease and *Helicobacter pylori* infection
- Identification of appropriate patients for *H. pylori* eradication treatment from among dyspeptic patients will entail a considerable investment of resources
- Consequently, the cost savings associated with a reduction in use of H₂ antagonists by patients who receive successful *H. pylori* eradication may take many years to materialise

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- Veldhuyzen van Zanten SJO, Sherman PM. Indications for treatment of *Helicobacter pylori* infection: a systematic overview. *Can Med Assoc J* 1994;150:189-98.
- Labenz J, Börsch G. Highly significant change of the clinical course of relapsing and complicated peptic ulcer disease after cure of *Helicobacter pylori* infection. *Am J Gastroenterol* 1994;89:1785-8.
- Bell GD, Powell KU, Bolton G, Richardson PDI. Clinical and pharmacoeconomic evaluation of management strategies for duodenal ulcer disease. *British Journal of Medical Economics* 1993;6:45-58.
- Campbell LM. The role of a *Helicobacter pylori* eradication regimen (omeprazole plus amoxycillin) in the long-term management of ulcer-like dyspepsia in general practice. *British Journal of Medical Economics* 1994;7:147-53.
- Sonnenberg A, Townsend WF, Miller AD. Evaluation of dyspepsia and functional gastrointestinal disorders: a cost-benefit analysis of different approaches. *European Journal of Gastroenterology and Hepatology* 1995;7:655-9.
- Edenholm M, Gustavsson R, Jansson O, Lingfors H, Nilsson O, Söderlind T, et al. Endoscopic findings in patients with ulcer-like dyspepsia. *Scand J Gastroenterol* 1985;20:163-7.
- Aldous J, Pryce D, Ramsay M. A pilot study of the effects of breath test screening and eradication of *Helicobacter pylori* on the management of dyspepsia in primary care. London: Academic Department of Public Health, St Mary's Hospital Medical School, 1994.
- Forrester E. Alternative advice on dyspepsia treatment. *Gastroenterology in Practice* 1994 Feb/Mar:6-7.
- Moore RA. *Helicobacter pylori and peptic ulcer*. Oxford: Health Technology Evaluation Association, 1995.
- Clausen MR, Franzmann MB, Holst C, Sørensen TIA, Christofferson P, Matzen P, et al. Longitudinal study of influence of *Helicobacter pylori* on current risk of duodenal ulcer relapse. *Scand J Gastroenterol* 1992;27:421-6.
- Axon ATR, Bell GD, Jones RH, Quine MA, McCloy RF. Guidelines on appropriate indications for upper gastrointestinal endoscopy. *BMJ* 1995;310:853-6.
- National Institutes of Health (NIH) Consensus Conference. *Helicobacter pylori* in peptic ulcer disease. *JAMA* 1994;272:65-9.
- Gribble EJ. The economics of a bug-free system. *Gastroenterology International* 1994;7:90.
- TreeAge Software. *DATA v2.6*. Boston: Treeware Software, 1995.
- Novell. *Quattro Pro v6.0*. Utah: Novello, 1995.
- Beck JR, Pauker SG. The Markov process in medical prognosis. *Med Decis Making* 1983;3:411-58.
- Sonnenberg FA, Beck R. Markov models in medical decision making: a practical guide. *Med Decis Making* 1993;13:322-38.
- Katz KD, Hollander D. Practical pharmacology and cost-effective management of peptic ulcer disease. *Am J Surg* 1992;163:349-58.
- Bardhan D. Refractory duodenal ulcer. *Gut* 1984;25:711-7.
- Logan RPH. Detection of *Helicobacter pylori* by the ¹³C-urea breath test. In: Rathbone BJ, Heatley RV, eds. *Helicobacter pylori and gastroduodenal disease*. 2nd ed. Oxford: Blackwell, 1992:88-106.
- Atherton JC, Spiller RC. The urea breath test for *Helicobacter pylori*. *Gut* 1994;34:723-5.
- Webb PM, Knight T, Greaves S, Wilson A, Newell DG, Elder J, et al. Relationship between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life. *BMJ* 1994;308:750-3.
- Kemmer TP, Dominguez-Muñoz JE, Klingel H, Zemmler T, Kuhn K, Malfertheiner P. The association between non-ulcer dyspepsia and *Helicobacter pylori* infection. *European Journal of Gastroenterology and Hepatology* 1994;6:571-7.
- HM Treasury. *Economic appraisal in central government: a technical guide for government departments*. London: HMSO, 1991.
- Briggs AH, Sculpher MJ, Buxton MJ. Uncertainty in the economic evaluation of health care technologies: the role of sensitivity analysis. *Health Econ* 1994;3:95-104.
- Patel P, Mendall M, Khulusi S, Mollineaux N, Levy J, Maxwell JD, et al. Salivary antibodies to *Helicobacter pylori*: screening dyspeptic patients before endoscopy. *Lancet* 1994;344:511-4.
- Sobala GM, Crabtree JE, Pentith JA, Rathbone BJ, Shallcross TM, Wyatt JL, et al. Screening dyspepsia by serology to *Helicobacter pylori*. *Lancet* 1991;338:94-6.
- Hastings L, Bell GD, Powell KU, Bolton C, Brown C, Sillis AJ, et al. Preliminary report on the impact of the Suffolk GP based *Helicobacter pylori* programme on the prescribing of ulcer healing drugs (UHDs) in general practice. *Gut* 1995;37(suppl 2):A6.
- Pym B, Sanstad J, Seville P, Byth K, Middleton WRJ, Talley NJ, et al. Cost-effectiveness of cimetidine maintenance therapy in chronic gastric and duodenal ulcer. *Gastroenterology* 1990;99:27-35.
- Bell GD, Powell KU, Bolton G, Richardson PDI. Reinfection of recrudescence after apparently successful eradication of *Helicobacter pylori* infection: implications for treatment of patients with duodenal ulcer disease. *Q J Med* 1993(b);86:375-82.
- Tytgat GNJ. Review article: treatments that impact favourably upon the eradication of *Helicobacter pylori* and ulcer recurrence. *Aliment Pharmacology and Therapeutics* 1994;8:359-68.
- Duggan AE, Knifton A, Logan RPH, Hawkey CJ, Logan RFA. Validation of two new rapid blood tests for *H. pylori*. *Gut* 1995;37:A58[Abstract].
- Netten A. *Unit costs of community care*. Canterbury: PSSRU, University of Kent, 1994.
- Chartered Institute of Public Finance and Accountancy. *Health database: health service trends. Vol 2. Detailed tables*. London: Health Service Management Association, 1990.
- Working Party of the Clinical Services Committee of the British Society of Gastroenterology. Provision of gastrointestinal endoscopy and related services for a district general hospital. *Gut* 1991;32:95-105.
- British Medical Association, Royal Pharmacological Society of Great Britain. *British National Formulary*. London: BMA Publishing, Royal Pharmacological Society of Great Britain, 1995.

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ANY QUESTIONS

For many years nursery and infant schoolchildren have been able to express their creativity using, among other things, cardboard tubes from toilet paper rolls. Now many schools will not accept these rolls "for health and safety reasons," presumably a fear of infection. Is this a sensible precaution or undue fussiness?

The impact of general hygiene on communicable disease control cannot be overemphasised. While infectious agents vary in mechanisms of pathogenicity and spread, transmission by contact is a mode common to most and hence the importance we place on proper hand washing in hospital practice. General hygiene is facilitated by the concept of "clean" and "contaminated" areas, practices, etc, and such principles should be encouraged in the

young. In addition, we know that bacteria and viruses from soiled hands can pass through several layers of toilet paper. The cardboard tube may become contaminated as the roll nears its end or from fingers holding the inside of the tube as paper is pulled off. For the above reasons and the potential for rapid spread of enteric diseases in nursery and infant schoolchildren I think that the cardboard tubes should not be used.—IAN K HOSEIN is a consultant medical microbiologist at the Public Health Laboratory Service in Cardiff

We welcome filler articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.