BMJ 2001;323:1066 (3 November)

Letters

Testing for *Helicobacter pylori* in dyspeptic patients

Did paper have statistical discrepancies?

EDITOR—I am confused by Weijnen et al's description of the statistical methods used in their study and how they fit with the data presented.[1] The methods section states that all variables found to be univariate predictors of peptic ulcer with P<0.25 were entered in the multivariate regression model. However, the results section says that age was included in the model, although table 2 shows that it was not predictive (P=0.67).

Table 2 also shows that P=0.24 for both hiatal hernia and pain after meal, so these should have been included in the multivariate model, but neither of them was. Are these discrepancies due to a typing mistake, or is there another explanation?

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1. Weijnen CF, Numans ME, de Wit NJ, Smout AJPM, Moons KGM, Verheij TJM, et al. Testing for Helicobacter pylori in dyspeptic patients suspected of peptic ulcer disease in primary care: cross sectional study. *BMJ* 2001; 323: 71-75[Abstract/Free Full Text]. (14 July.)

Authors' suggestion muddies waters in debate

EDITOR—Weijnen et al suggest that we should test and treat patients at high risk of peptic ulceration.[1] This seems to muddy the waters in the debate about testing for *Helicobacter pylori* infection in primary care. Of the 38 patients they identified as having

a peptic ulcer, only 22 gave a positive result to a non-invasive *H pylori* test, although the rate of detection overall was increased from 31% to 41% by using invasive tests of culture or histology, which suggests that serological testing is not as sensitive.

Agreus and Talley reported that the sensitivity of *H pylori* enzyme linked immunosorbent assay (ELISA) kits had an average sensitivity of 85% (low and high extremes 49% and 99% respectively).[2] Why are the rates of detection so low in Weijnen et al's study (33 of the 38 patients had a duodenal ulcer), when it has been shown that virtually all patients with a duodenal ulcer have *H pylori* infection?[3] This apparent discrepancy will make it difficult to generalise their results into primary care.

My practice will continue to follow the recommendations in *Guidelines* (a free publication to all general practitioners), which summarises current evidence.[4] This gives a suggestion from the Primary Care Society for Gastroenterology: that routine testing of patients with dyspepsia that has not been investigated is not recommended at the first presentation, but at subsequent presentations testing and referral for endoscopy are appropriate.

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1. Weijnen CF, Numans ME, de Wit NJ, Smout AJPM, Moons KGM, Verheij TJM, et al. Testing for Helicobacter pylori in dyspeptic patients suspected of peptic ulcer disease in primary care: cross sectional study. *BMJ* 2001; 323: 71-75[Abstract/Free Full Text]. (14 July.)
2. Agreus L, Talley N. Challenges in managing dyspepsia in general practice. *BMJ* 1977; 315: 1284-1288[Free Full Text].
3. Blaser M. Helicobacter pylori and the pathogenesis of gastroduodenal ulceration. *J Infect Dis* 1990; 162: 623-633.
4. Ford-Kelcey G, ed. *Guidelines. Summarising clinical guidelines for primary care.* Berkhamsted: Medendium Group, 1999.

Authors' strategy would leave many patients with ulcer uncured

EDITOR—Weijnen et al recommend that use of the *Helicobacter pylori* test should be restricted to dyspeptic patients with a history indicating a high risk of underlying ulcer.[1] This would include patients with a history of peptic ulcer and those who were smokers and experienced pain on an empty stomach.

Their recommendation is based on their finding that the prevalence of underlying ulcer in such patients with a positive result of an *H pylori* test was 26%, compared with only 7% in their other dyspeptic patients with a positive result. We agree that the proposed strategy is attractive in reducing the number of patients treated with antibiotics per ulcer cured. But because of the insensitivity of clinical history in predicting ulcers it will deprive a substantial proportion of dyspeptic patients of a simple long term cure of their underlying ulcer. Indeed, the paper shows that the strategy would leave 36% of the patients with ulcer who were positive for *H pylori* uncured of their chronic disease, at risk of subsequent ulcer complications, and requiring long term acid inhibitory treatment.

We also disagree with the authors' assertion that the likelihood of underlying ulcer is the only factor in favour of treating *H pylori* infection in dyspeptic patients. Benefits of treating the infection in patients without ulcer include curing symptoms in 9% of such patients,[2] removing their recognised increased risk of subsequent ulcer,[3] removing a recognised risk factor for gastric cancer and lymphoma,[4] and removing the risk of the patient developing atrophic gastritis with subsequent proton pump inhibitor treatment.[5]

For the above reasons, it seems inappropriate to restrict the *H pylori* test and treat strategy to patients whose history indicates a higher risk of ulcer.

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1. Weijnen CF, Numans ME, de Wit NJ, Smouth AJPM, Moons KGM, Verheij TJM, et al. Testing for Helicobacter pylori in dyspeptic patients suspected of peptic ulcer disease in primary care: cross sectional study. *BMJ* 2001; 323: 71-75[Abstract/Free Full Text]. (14 July.)
2. Moayyedi P, Soo S, Deeks J, Forman D, Mason J, Innes M, et al, on behalf of the Dyspepsia Review Group. Systematic review and economic evaluation of Helicobacter pylori eradication treatment for non-ulcer dyspepsia. *BMJ* 2000; 321: 659-664[Abstract/Free Full Text].
3. McColl KEL. Should we eradicate Helicobacter pylori in non-ulcer dyspepsia? *Gut* 2001; 48: 759-761[Free Full Text].
4. Blum AL, Talley NJ, O'Morain C, Veldhuyzen van Zanten S, Labenz J, Stolte M, et al. Lack of effect of treating Helicobacter pylori infection in patients with non-ulcer dyspepsia. *N Engl J Med* 1998; 339: 1875-1881[Abstract/Free Full Text].
5. Kuipers EJ, Lundell L, Klinkenberg-Knol EC, Havu N, Festen HPM, Liedman B, et al. Atrophic gastritis and Helicobacter pylori infection in patients with reflux esophagitis treated with omeprazole or fundoplication. *N Engl J Med* 1996; 33: 1018-

1022[CrossRef].

Clinical importance of predictive values is dubious

EDITOR—Weijnen et al stated that testing for *Helicobacter pylori* in dyspeptic patients provided additional diagnostic information in patients deemed to have a high risk of peptic ulcer.[1] Closer scrutiny of table 4 shows that the test actually performed similarly in the low and high risk groups. Positive likelihood ratios calculated for the two groups are 1.8 (95% confidence interval 1.1 to 3.1) and 1.8 (1.2 to 2.7) respectively. The negative likelihood ratios were 0.7 (0.4 to 1.1) and 0.6 (0.3 to 1.0) respectively.

If a prevalence of 16% is assumed for peptic ulcer this equates to a post-test probability of 18.6% to 34% if the confidence interval for the positive likelihood ratio in the high risk group is used. If the test result was negative in this group the post-test probability would be 5.4% to 16%. On the basis of this the test adds little further information to that obtained by history taking. The authors do not state whether the changes in predictive values (16% to 26% and 16% to 10%) were significant, but their clinical importance, in terms of diagnosing peptic ulcer, seems dubious even for the high risk group.

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1. Weijnen CF, Numans ME, de Wit NJ, Smout AJPM, Moons KGM, Verheij TJM, et al. Testing for Helicobacter pylori in dyspeptic patients suspected of peptic ulcer disease in primary care: cross sectional study. *BMJ* 2001; 323: 71-75[Abstract/Free Full Text]. (14 July.)

Authors' reply

EDITOR—Jacobs is confused by our criteria for including predictors in the multivariate analysis. Multivariate analysis was performed with all variables of P<0.25 in univariate analysis plus variables that are considered clinically relevant and were important predictors in earlier studies.[1] For the latter reason age was selected for multivariate analysis and not because it was associated with peptic ulcer, as stated in the second paragraph of the results section. Hiatal hernia and pain after meal should also have been mentioned here as they were also selected for multivariate analysis on the basis of their univariate P value of P<0.25.

We do not agree with Williams that our results muddy the waters of guidelines for *Helicobacter pylori* testing. We do not believe that the relatively low *H pylori* infection rate in our patients with duodenal ulcer is due to poor test performance; a trend towards *H pylori* negative duodenal ulcers in countries with low infection rates has been reported previously.[2] This means that the role of *H pylori* testing in primary care management of peptic ulcer needs closer consideration; we aimed at defining more precisely the diagnostic contribution of testing to finding cases.

We agree with McColl and Murray that applying our strategy to all dyspeptic patients would mean that a minority of the patients with *H pylori* infection and ulcer would not immediately be treated optimally. As the evidence base for testing and treating all dyspeptic patients is poor and prompt endoscopy in all cases is unrealistic, we think our algorithm represents the best compromise between overtreatment and optimal treatment for patients with ulcer in primary care. We realise that many colleagues consider *H pylori* treatment beneficial for several other indications. So far, however, the effectiveness of this treatment has not been shown in these patients.

Sultana comments that the additional effect of the *H pylori* test is limited, and wonders whether the change from prior to posterior probability was significant. In the high risk group these changes after a positive test (from 16% to 26%) and a negative test (from 16% to 10%) were significant, as is also indicated by the 95% confidence intervals of the two posterior probabilities estimated by Sultana. In the low risk group no significant changes were seen. In addition, the cost effectiveness of *H pylori* testing in the high risk group compared with the overall group is much higher (40 out of 54 *v* 152 out of 174 treated unnecessarily). This underlines the clinical value of *H pylori* testing in the high risk group only.

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Related Article

Testing for *Helicobacter pylori* in dyspeptic patients suspected of peptic ulcer disease in primary care: cross sectional study

Catherine F Weijnen, Mattijs E Numans, Niek J de Wit, André J P M Smout, Karel G M Moons, Theo J M Verheij, and Arno W Hoes
BMJ 2001 323: 71-75. [Abstract] [Full Text]