(such as age and social class) are found to be associated, even after adjustment, it seems sensible to treat such associations with caution until evidence of causality can be obtained—in this case from a prospective randomised controlled trial of the eradication of *H pylori* infection. We therefore believe that eradication of *H pylori* infection on the grounds of the risk of cardiovascular disease alone, like that of gastric cancer alone,[4] is not supported by the current evidence.

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1 Patel P, Mendall MA, Carrington D, Strachan DP, Leatham E, Molineaux N, *et al.* Association of Helicobacter pylori and Chlamydia pneumoniae infections with coronary heart disease and cardiovascular risk factors. *BMJ* 1995;311:711-4. (16 September.)
2 Delaney BC, Kenkre JE, Hobbs FDR. A whole blood NPT for antibodies to H pylori: effect on the management of dyspepsia in primary care [abstract]. *Fam Pract* 1995;12:263-4.
3 Webb PM, Knight T, Greaves S, Wilson A, Newell DG, Elder J, *et al.* Relation between infection with Helicobacter pylori and living conditions in childhood: evidence for person to person transmission in early life. *BMJ* 1994;308:750-3.
4 EUROGAST Study Group. An international association between Helicobacter pylori infection and gastric cancer. *Lancet* 1993;341:1359-62.

Authors' reply

EDITOR,—Brendan C Delaney and colleagues point out that the association between seropositivity for antibodies to *Helicobacter pylori* and coronary heart disease (based on history alone) in our study failed to reach significance. It is more important, however, to look at the odds ratio and confidence interval. We suggest that an odds ratio of 1·87 (95% confidence interval 0·87 to 4·02) is important in a common disease like coronary heart disease.

The reason for Delaney and colleagues' failure to find an association between *H pylori* infection and a history of ischaemic heart disease (as ascertained from general practice records) is unclear, but selection bias may have been a problem as the subjects were all attending their general practice. In any event, the confidence interval for the odds ratio that they observed (0·63 (0·32 to 1·26)) overlaps ours. An association of a similar magnitude to that observed in our study has been reported recently in a large population based study of 2000 subjects aged 25-65 that used the Rose angina questionnaire to define coronary heart disease. The odds ratio for *H pylori* infection in patients with coronary heart disease as defined by the questionnaire was 1·68 (0·89 to 3·10) in men after adjustment for age, smoking, and social class.[1] Furthermore, the association between *H pylori* infection and coronary heart disease was shown in patients with disease evident on angiography in our original study[2] and in patients with myocardial infarction in another study.[3]

With regard to the predictive value of electrocardiographic findings of coronary heart disease, we would refer Delaney and colleagues to the Whitehall study, in which the abnormalities we chose were validated in relation to subsequent death from coronary heart disease.[4] Most electrocardiographic abnormalities involved Q waves (22 patients had *H pylori* infection out of 26 with Q wave abnormalities). Rates of infection in those with ST depression (5/6), T wave inversion (7/11), and left bundle branch block (2/4) were slightly lower, possibly reflecting the reduced specificity of these abnormalities for coronary heart disease.

The relation between *H pylori* and *Chlamydia pneumoniae* infection and coronary heart disease was assessed by logistic regression models with the outcome variables being, in turn, history of angina or myocardial infarction; electrocardiographic evidence of ischaemia or infarction; and prevalent coronary heart disease (defined as either a history of the disease or electrocardiographic evidence of it). In the model *H pylori* and *C pneumoniae* infections were individually treated as dichotomous variables (0,1) and no separate term for both infections was included as they correlated with each other weakly (as shown in table I in our paper). Furthermore, there was no evidence of statistical interaction between *H pylori* and *C pneumoniae* infection as suggested by the unadjusted data, nor was there an a priori biological reason to suspect this.

Delaney and colleagues are incorrect in saying that generalised linear interactive modelling gives inaccurate results for logistic regression when there are few results in a particular group. The validity of unconditional estimates of regression variables depends on whether the number of variables fitted approaches the total number of independent observations (study subjects). In our study this ratio was less than 10%.

We appreciate the comment on confounding by age and social class, but residual confounding was unlikely or small because there was little difference in the odds ratio after adjustment. Finally, we agree (as we stated clearly in our paper) that further studies including interventional and prospective trials need to be carried out to address this issue further.

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1 Murray LJ, Bamford KB, O'Reilly DPJ, McCrum EE, Evans AE. Helicobacter pylori infection: relation with cardiovascular risk factors, ischaemic heart disease, and social factors. *Br Heart J* 1995;74:497-501.
2 Mendall M, Goggin P, Levy J, Molineaux N, Strachan D, Camm A, *et al.* Relation of Helicobacter pylori infection and coronary heart disease. *Br Heart J* 1994;71:437-9.
3 Martin-de-Argila C, Boixeda D, Canton R, Gisbert JP, Fuertes A. High seroprevalence of Helicobacter pylori infection in coronary heart disease. *Lancet* 1995;346:310.
4 Rose G, Baxter PJ, Reid DD, McCartney P. Prevalence and prognosis of electrocardiographic findings in middle-aged men. *Br Heart J* 1978;40:636-43.

Increasing prescription of drugs for secondary prevention of myocardial infarction

Authors' recommendations are too restrictive

EDITOR,—Janet Smith and Kevin S Channer state that "there are few published data on the efficacy of multiple combinations for secondary prophylaxis" after acute myocardial infarction.[1] Consequently, they recommended to colleagues the long term use of aspirin and one other drug. We assume that the second drug was most commonly either a β blocker or an angiotensin converting enzyme inhibitor. We believe that this commonly adopted approach is much too restrictive.

The Norwegian timolol trial[2] and the β blocker heart attack trial of propranolol[3] reported a major survival benefit in patients with clinical evidence of heart failure. Indeed, the criteria used to define this subgroup in the β blocker heart attack trial formed the basis of the inclusion criteria in the acute infarction ramipril efficacy study.[4] Furthermore, in the latter study, as with the other trials of angiotensin converting enzyme inhibitors, at least a quarter of patients selected for treatment were receiving a β blocker at the time of randomisation.[5] This subgroup also showed a sizeable reduction in all cause mortality as a result of treatment with an angiotensin converting enzyme inhibitor. Taken with similar findings in the survival and ventricular enlargement trial and the trandolapril cardiac evaluation study,[6] these data strongly support the use of both agents in some patients.

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1 Smith J, Channer KS. Increasing prescription of drugs for secondary prevention after myocardial infarction. *BMJ* 1995; 311: 917-8. (7 October.)
2 Norwegian Multicentre Study Group. Timolol-induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction. *N Engl J Med* 1981;304:801-7.
3 Beta-blocker Heart Attack Trial Research Group. A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. *JAMA* 1982;247:1707-14.
4 Hall AS, Winter C, Bogle SM, Mackintosh AF, Murray GD, Ball SG. The acute infarction ramipril efficacy (AIRE) study: rationale, design, organization, and outcome definitions. *J Cardiovasc Pharmacol* 1991;18(suppl 2):S105-9.
5 Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. *Lancet* 1993;342:821-8.
6 Køber L, Torp-Pedersen C, Carlsen JE, Bagger H, Eliasen P, Lyngborg K, *et al* for the Trandolapril Cardiac Evaluation (TRACE) Study Group. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 1995;333:1670-6.

Lipid lowering drugs should be considered too

EDITOR,—Janet Smith and Kevin S Channer describe the lack of translation into clinical practice of evidence from trials of secondary prevention of myocardial infarction.[1] It is notable that lipid lowering interventions were not included in the list of treatments used for secondary prevention. While further definitive evidence of the effect on total mortality of lowering cholesterol concentrations in this context was published recently,[2] a considerable number of studies—for example, the St Thomas's atherosclerosis regression study[3]—have shown regression of coronary atherosclerosis, and meta-analysis has shown a reduction in mortality from coronary heart disease.[4] The problem of objectivity in discussions of drug interventions in cardiovascular disease has been described before.[5]

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1 Smith J, Channer KS. Increasing prescription of drugs for secondary prevention after myocardial infarction. *BMJ* 1995; 311:917-8. (7 October.)
2 Scandinavian Simvastatin Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian simvastatin survival study (4S). *Lancet* 1994;344:1383-9.
3 Watts GF, Lewis B, Brunt JNH, Lewis ES, Coltart DJ, Smith LDR, *et al.* Effects on coronary heart disease of lipid-lowering diet, or diet plus cholestyramine, in the St Thomas' atherosclerosis regression study (STARS). *Lancet* 1992;339:563-9.
4 Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ* 1994;308: 367-72.
5 Durrington PN, Bhatnagar D. Wrong lesson from Finnish trial of cardiovascular disease prevention. *Lancet* 1992;339:488.

Managing cleft lip and palate

EDITOR,—The letters[1] commenting on Tony Markus and Peter Ward Booth's editorial on the management of cleft lip and palate[2] raise the spectre of two surgical specialties at public loggerheads. Unfortunately, the dispute has had important consequences for those who should be able to