transdermal nicotine patches before marketing them. The patients with heart disease who participated were kept under strict cardiovascular control. Many cases of angina pectoris and arrhythmias were reported, which led to patients being withdrawn from the study, being admitted to hospital, and even undergoing angioplasty. The study concluded that patches are safe only in patients with stable cardiovascular disease.⁴

The pharmacological effects of nicotine (regardless of its source) on the cardiovascular system are well known.

(1) Nicotine increases blood pressure and heart rate directly, because it has sympathomimetic effects on the heart, and indirectly, because it stimulates catecholamine release. These effects increase myocardial oxygen demands, risking the development of angina pectoris due to reversible myocardial ischaemia, especially in patients with coronary stenosis.

(2) It causes vasospasm in coronary vessels because of its sympathomimetic effects and because it stimulates the local release of prostaglandins.

(3) It may cause platelets to hyperaggregate and increase blood fibrinogen concentrations, which increase the risk of coronary thrombosis and myocardial infarction.

In addition, the drug interactions of propranolol and the contraceptive pill with nicotine should be considered as they might increase nicotine blood concentrations unexpectedly.⁵

The pharmacological effects of nicotine on the cardiovascular system need to be carefully investigated in patients with heart disease who use transdermal nicotine patches. Currently, the safety of such patients using them depends on continuous supervision by a physician, especially in those with coronary stenosis or a history of myocardial infarction.

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1 McMurray J, Rankin A. Recent advances in cardiology. I. Treatment of myocardial infarction, unstable angina, and angina pectoris. *BMJ* 1994;309:1343-50. (19 November.)

2 Warner JG, Little WC. Myocardial infarction in a patient who smoked while wearing a nicotine patch. *Ann Intern Med* 1994;120:695.

3 Cardiale problemen bij toepassing van nicotine pleisters. *Geneesmiddelen Bulletin (prik board)* 1994;28(8):28. (In Dutch.)

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Authors' reply

EDITOR,—As discussed by John Rawles and us,^{1,2} analysis of the "early thrombolysis" trials, and not just the Fibrinolytic Therapy Trialists' overview, suggests that giving thrombolysis 60 minutes earlier, a generally feasible time saving, will probably save at least 15 additional lives per 1000 patients treated. This conclusion is much less controversial than how the results of the GUSTO trial (global utilisation of streptokinase and tissue plasminogen activator for occluded arteries) should be interpreted. This controversy was reviewed by us, but two points should be emphasised.

Firstly, Anthony Hall and D M Humphreys fail to point out that the GUSTO trial was not just a comparison of two drugs. It was also a trial of strategies, in which one thrombolytic agent was given rapidly (accelerated alteplase) and the other (streptokinase) at the usual rate.

Secondly, the analysis reported by Hall and Humphreys puts streptokinase at a disadvantage. Accelerated alteplase (currently not licensed in the United Kingdom) is compared with the combined

Numbers of patients who need to be treated to prevent one event

Treatment	Event prevented	No of patients who need to be treated to prevent one event
Of hypertension*	Death, cerebrovascular accident, myocardial infarction	3
Coronary artery bypass grafting for left main stem stenosis	Death	3
Aspirin for transient ischaemic attack	Death, cerebrovascular accident	6
Warfarin for atrial fibrillation	Cerebrovascular accident	7
ACE inhibitor for mild heart failure	Death, admission to hospital	8
After myocardial infarction:		
HMG CoA reductase inhibitor	Death, myocardial infarction, cardiac arrest	11
Aspirin	Death, myocardial infarction, cerebrovascular accident	12

*Diastolic pressure 115-129 mm Hg.
ACE=Angiotensin converting enzyme.

HMG CoA=Hydroxymethyl glutaryl coenzyme A.

streptokinase groups. When given with intravenous heparin (a non-standard treatment), streptokinase caused more strokes and bleeding complications; these complications were less frequent when streptokinase was combined with subcutaneous heparin. It would be more valid to compare the combined death rate and rate of non-fatal disabling stroke (the stroke rate was increased by alteplase) in the accelerated alteplase group with that in the streptokinase and subcutaneous heparin group (6.9% v 7.7%, $P=0.03$).

Even if we accept the analysis of Hall and Humphreys the number of patients that need to be treated to save one life by using alteplase rather than streptokinase is around 100 (though the 95% confidence limits are as high as 240).³ In other words, the cost per extra life saved is of the order of £67 000 but could be as much as £160 000. To this must be added the not inconsiderable cost of an extra disabling stroke. The opportunity cost of routinely switching from streptokinase to alteplase would, consequently, be significant. We cannot agree, therefore, that the cost of the extra benefit from alteplase is small compared with other treatments, even angioplasty (table). We believe that it is entirely appropriate to place these issues in the context of the extra benefit that could be obtained, at no extra cost, by improving current practice to ensure that thrombolysis is given as early as possible.

We did not wish to imply that transdermal nicotine replacement treatment is completely safe in patients with coronary heart disease. Instead we concluded that the role of nicotine replacement in helping patients to stop smoking after a myocardial infarction should be explored further. We still think that this is the case. The study we cited is a double blind placebo controlled five week trial in 156 patients and is, therefore, of considerable value. May R Arnaot, however, cites only individual case reports as evidence against the safety of nicotine replacement treatment. Few such cases have been reported to the United States Food and Drugs Administration.⁴

Arnaot summarises the well known effects of nicotine on the cardiovascular system. Nicotine itself, however, has less pronounced effects than smoking on some of these variables.⁴ Concomitant smoking should ideally be avoided and only patients whose condition is stable should be considered for treatment. We think, however, that the role of nicotine replacement as an aid to smoking cessation in survivors of myocardial infarction should not be dismissed without fuller evaluation.

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1 Rawles J. Treatment of myocardial infarction and angina. *BMJ* 1995;310:465. (18 February.)

2 McMurray J, Rankin A. Treatment of myocardial infarction and angina. *BMJ* 1995;310:465. (18 February.)

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4 Orleans CT, Resch N, Noll E, Keintz MK, Rimer BK, Brown TV, et al. Use of transdermal nicotine in a state-level prescription plan for the elderly. *JAMA* 1994;271:601-7.

GPs accept patients' vote on fundholding

EDITOR,—My partners and I were interested to read of the ballot of patients in a practice in Oxfordshire over whether their practice should become a fundholding practice.¹ Our patient participation group, in association with Leicestershire Family Health Services Authority, funded and carried out a similar exercise in 1991. I write not to claim a first but to compare the outcome.

The fundholding facilitator of the family health services authority and the patient participation group's committee agreed a foreword to the voting paper, explaining the pros and cons of fundholding. No indication of the general practitioners' views was given. The voting papers were sent to a 10% random sample (chosen by the family health services authority) of our adult patients. All voting papers were anonymous and were returned in prepaid envelopes.

Altogether 850 papers were distributed; 372 were returned. The number of patients in favour of the practice becoming a fundholding practice was 108, with 262 against (two spoilt papers)—that is, 70% of the respondents were against fundholding for the practice. The commonest reason against fundholding was the problem of patients' confidence in their doctors' decisions once money had entered into the equation.

Our practice did not become fundholding, and we have seen no reason since then to change our minds.

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1 Leaver M. GPs accept patients' vote on fundholding. *BMJ* 1995;310:349-50. (11 February.)

Reductions in defence medical services

EDITOR,—While fully understanding the concern expressed by the BMA's armed forces committee over the proposed changes in the medical defence services, I cannot accept that the changes will have an "adverse effect on the quality of care which will be offered to serving personnel in the future."¹ In addition, the statement that doctors are unlikely to be recruited on short career commissions in the future is not correct. There will be a full and rewarding career in the, albeit smaller, armed forces medical service of the future, and short term commissions will, as at present, form the bedrock of our recruiting policy.