the person who wrote the advance directive is ridiculous. The courts are used to dealing with normal wills and have a good grasp of testamentary capacity. They accept an earlier will if later ones are seen to have been affected by mental illness or cerebral disorder. Clearly, the courts take the view that the person owning the estate was the person who existed before the onset of mental or cerebral illness. I consider that I own my body and my life. I would wish to specify the disposition of them while I am of sound mind, subject to rigid safeguards.

I am constantly saddened by the arrogance of those who wish to impose their beliefs and their analysis of situations on others. I have no wish to force Robertson to make an advance directive. I wish he would not try to deprive me of the right to do so.

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Prejudice against Basildon is unwarranted

EDITOR,—I imagine that the *BMJ* welcomes debate in its letter columns to guide its editorial policy, but I was disappointed by K Cleary's letter about classified advertisements, which focuses on examples of content that were irrelevant.¹ Cleary reasonably censures one inept medical recruitment department for errors in an advertisement and another for being economical with the truth concerning financial inducements. Cleary's prejudices about Basildon, however, are inappropriate. There is nothing wrong with working in Basildon, Hackney (as Cleary does), or anywhere else. Basildon Hospital is evolving into an important non-metropolitan teaching hospital for undergraduates and postgraduates. Its high profile advertisements are meant to be original and the content sincere. This month the chief medical officer will give the opening lecture at an expanded £500 000 postgraduate education centre with a new state of the art lecture theatre. A unique local professional trust fund advertises in the *BMJ* for research projects (applicants are mainly trainees) and awards grants of up to £25 000 a year.

At a time when I am extremely concerned about recruitment of consultant psychiatrists generally, I deprecate my psychiatric colleague's slur on the medical staff in this district, who take the recruitment of good consultants very seriously indeed.

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1 Cleary K. Classified advertisements in the *BMJ*. *BMJ* 1995;311:1027. (14 October.)

Government health warnings may encourage adolescents to smoke

EDITOR,—Despite an intensive antismoking campaign aimed at young people and a decreasing prevalence of smoking among adults the prevalence of smoking in adolescents is increasing.^{1,2} I suggest that one possible contributor to this disturbing trend is government health warnings.

There is no evidence that health warnings deter adolescents from smoking,³ but there are several reasons why they may produce the opposite effect.

Adolescents take up smoking to rebel, to show proof of daring, to feel grown up, and to conform with their peers.³ Government health warnings make it easier for adolescents to achieve all of these. Health warnings are the recurring voice of a disapproving establishment. They emphasise the element of risk, they reinforce a subliminal association between smoking and adulthood, and they provide a banner under which, subconsciously, all adolescent smokers can unite.

The voluntary agreement between the government and the tobacco industry states that advertisements for cigarettes cannot show material that suggests it is daring to smoke or that would appeal to those who are rebellious, particularly the young. On these grounds, should not all cigarette advertisements carrying a health warning be banned?

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- 1 Diamond A, Goddard E. *Smoking among secondary school children in 1994*. London: HMSO, 1995.
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Misleading meta-analysis

One incorrect meta-analysis does not invalidate them all

EDITOR,—Guilt by association is dangerous practice in medicine as in law, yet James Le Fanu seeks to discredit the results of all meta-analyses¹ because of the incorrect result of one: small trials of intravenous magnesium in acute myocardial infarction suggested an effect not confirmed by a large trial.² The misleading suggestion was probably due to publication bias.² Meta-analyses are not immune to error and must be evaluated as critically as individual studies.

Le Fanu considers that passive smoking does not cause lung cancer. It is acknowledged that exposure to carcinogens has no threshold below which there is no effect. Linear dosimetry indicates an excess risk of about 20% in exposed compared with unexposed non-smokers (exposure from passive smoking is about 1% of that from actively smoking 20 cigarettes daily,³ which conveys about a 20-fold excess risk). Meta-analysis of the epidemiological studies, updated, gives about the same result.³ This consistency from two independent sources indicates that the estimate of 20% is about right. Variation in the distribution of the sites of cancers in the lung, with a higher proportion of peripheral cancers in passive smokers, is not surprising, as the source cited by Le Fanu indicated.

Le Fanu states that the effect of salt on blood pressure is "very small." Our analysis estimated that a reduction in daily salt intake of 3 g (30-40%) at age 50-59 lowers systolic blood pressure by 5 mm Hg, which is equivalent to a decrease of 22% in mortality from stroke and 15% in mortality from heart disease.⁴ The effect on blood pressure may seem small, but the effect on disease is great. The accuracy of the estimates of the effect of salt on blood pressure was confirmed by the precise prediction of the reductions in blood pressure (ranging from 2.6 to 25.2 mm Hg) in each of the 33 trials of salt reduction previously reviewed⁴ when the mean initial blood pressure, age, and reduction in salt intake in each trial were taken into account. Le Fanu attributes the blood pressure lowering in trials of salt reduction to a placebo effect; the precise prediction of the results of the double blind trials (not susceptible to placebo effect) refutes this possibility.⁵

Le Fanu's "biological common sense" might best be described as his personal opinion. Indeed, common sense supports the evidence. Breathing carcinogens from environmental tobacco smoke causes lung cancer but to a proportionately lesser extent than inhaling the carcinogens from active smoking. Salt, known to increase blood pressure experimentally, does so as expected in the general population.

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Subject to many potential biases

EDITOR,—I M Anderson and B M Tomenson's paper¹ updates our meta-analysis comparing drop out rates in patients taking selective serotonin reuptake inhibitors and tricyclic antidepressants² but excludes newer tricyclic drugs. Despite this difference, which would tend to favour the selective serotonin reuptake inhibitors, the results are nearly identical. The table compares drop out rates in the three published meta-analyses.^{1,3} Clearly, despite the different inclusion criteria, the results broadly agree: the difference is small and of dubious clinical and economic importance.

Drop out rates among patients taking selective serotonin reuptake inhibitors and tricyclic antidepressants in three meta-analyses

	Drop out rate (%)		
	Selective serotonin reuptake inhibitors	Tricyclic anti-depressants	Absolute difference (%)
Song <i>et al</i> ⁴	32.3	33.2	0.9
Montgomery <i>et al</i> ⁵ *	33.8	35.6	1.8
Anderson and Tomenson ¹	30.8	33.4	2.6

*Calculated from figures in paper, with correction for errors.

The small absolute difference found in these meta-analyses may be a poor estimate of the actual difference in drop out rates, for several reasons. Firstly, in several studies patients who were entered into the trials had already failed to benefit from a previous course of tricyclic drugs, and this can bias the results against these drugs. Secondly, seven relevant studies were excluded from Anderson and Tomenson's meta-analysis because the total number of drop outs was not reported. This may result in a bias if drop out rates were not reported because they did not show selective serotonin reuptake inhibitors to be significantly better tolerated. Thirdly, the different clinical settings of the trials may also bias the results. Finally, most studies have a follow up of four to six weeks; in practice, longer treatment is usually recommended.⁴

The broad agreement in the main, albeit crude, outcomes examined by the three meta-analyses shows the strength of our initial conclusion that the routine prescription of selective serotonin reuptake inhibitors as the first line treatment of depression cannot be justified by analysis of the available data.

Further reanalysis of existing trials is unlikely to yield new insights, which will require new studies. Anderson and Tomenson recommend investigation of antidepressants prescribed in clinical practice rather than in clinical trials. Such observational studies are subject to many potential biases, which reduce the validity of comparisons.³ What is needed are large, well designed pragmatic randomised controlled trials in primary care settings; such trials will allow both reliable and generalisable estimation of the relative effectiveness and cost effectiveness of different classes of antidepressants, as used in routine clinical practice and over a longer period. Future randomised controlled trials comparing classes of antidepressants should also use more relevant outcomes to measure quality of life in those who continue to use treatments and those who drop out.

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Exercise responses in the chronic fatigue syndrome

Objective assessment of study is difficult without knowledge of data

EDITOR,—In their study of exercise responses and psychiatric disorder in the chronic fatigue syndrome Russell J M Lane and colleagues claim to have detected abnormal lactate responses to subanaerobic threshold exercise in 31 of 96 patients.¹ As no data are offered to support this statement, however, objective assessment of the validity of their findings is difficult.

The authors' definition of an abnormal response is "lactate concentrations exceeding the upper 99% reference limit for normal control subjects at two or more time points." However, only three samples were taken (before, immediately after, and 30 minutes after exercise), and a raised lactate concentration in the sample obtained before exercise began cannot be described as an abnormal response to exercise. Neither the method used to measure lactate nor its precision is given; assessment of the importance of the "abnormal" lactate concentrations could not be guessed at without this information, even if the authors had given details of the patients' concentrations.

Finally the "normal" ranges were published six years ago in a study in which patients and controls were not matched.² Lactate responses to exercise are notoriously difficult to interpret in isolation, and since the early studies of Pearson *et al* into McArdle's disease³ it has been standard practice in this type of study to run a parallel test in a control matched for age, sex, and weight⁴; this does not

seem to have been done in Lane and colleagues' study.

I believe that it is impossible to verify the authors' conclusions without seeing their data, and I am surprised that they were not included.

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Authors' reply

EDITOR,—The constraints on the number of words in a short report prevented us from giving the lactate concentrations. In the 31 patients with a positive response to the subanaerobic threshold exercise test, concentrations exceeded the upper 99% confidence interval established in normal control volunteers in the paper by Nashef and Lane,¹ cited by Alan S Hutchison, in 28 subjects before exercise and in 29 subjects immediately after and in 29 subjects 30 minutes after exercise. Before November 1990 the plasma lactate concentration was measured with a Sigma kit, as detailed by Nashef and Lane. Since then the concentration has been measured with a Stat lactate analyser (Yellow Springs Instrument, Ohio). The table shows the precision data between batches for two periods in which these methods were used; the data are based on internal quality control samples run with each batch of assays.

Precision data for two assays measuring lactate concentration, 1989-95

	Dec 89-Oct 90	Aug 94-Feb 95
No	42	42
Mean (SD) (mmol/l)	2.31 (0.12)	2.25 (0.16)
Coefficient of variation (%)	5.1	7.1

To some extent we share Hutchison's reservations regarding the validity of the confidence intervals for lactate concentrations based on historical controls. Nevertheless, the subanaerobic threshold exercise test largely eradicates variations related to age, sex, and weight.² We would have been more concerned if the majority of patients with the chronic fatigue syndrome had shown abnormal results: the upper limit of the confidence interval might have been artificially low. However, results were normal in two thirds of cases.

The point concerning the baseline lactate concentrations is pedantic. A raised resting concentration is abnormal and might indicate defective mitochondrial function, for example.² The issue of lactate responses to exercise in glycogenoses is not really pertinent. Here, one is looking for a partial or complete lack of increase in lactate concentration after ischaemic exercise of a limb. Control of factors such as the intensity and duration of work and procedures for collecting samples must be much more stringent.³

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Volume and mortality in coronary artery bypass grafting

EDITOR,—Amanda J Sowden and colleagues' meta-analysis of six studies of the relation between the volume of coronary bypass graft surgery performed and mortality concludes that the relation is less apparent with better adjustment for case mix and has become attenuated over time.¹ Unfortunately, in the one study with clinical risk factors, which was also the most recent one and was carried out in New York, 96.7% of all patients were treated in the 26 (out of 30) hospitals with >200 cases. This makes it difficult to detect a volume effect in this study. Without additional studies with clinical risk factor models from other times and places it is impossible to test the authors' hypotheses.

We have addressed the question of a time trend, looking at Californian data for 1983-9. Adjusted death rates by volume of coronary artery bypass grafting were estimated with a risk model based on data from discharge abstracts.² (Although better risk models may alter these results, they largely reflect substantial differences in mortality rather than in expected rates; predicted risk falls with volume up to about 250 cases a year and is flat thereafter.) Following the method of Sowden and colleagues, we used logistic regression to estimate odds ratios between volume and adjusted risk of death for each year and to determine whether the relation between volume and outcome changed over time. We found significantly lower death rates adjusted for risk in high volume hospitals for each year except 1983 (1983, odds ratio 0.87 (95% confidence interval 0.73 to 1.04); 1984, 0.83 (0.71 to 0.99); 1985, 0.70 (0.60 to 0.81); 1986, 0.77 (0.67 to 0.88); 1987, 0.82 (0.71 to 0.94); 1988, 0.85 (0.74 to 0.96); 1989, 0.85 (0.74 to 0.97)). The interaction of year and volume was not significant. Furthermore, in California the proportions of both hospitals and patients in high volume hospitals were far lower than those in New York and fell during the period, from 54% to 32% and from 78% to 62% respectively.

The figure shows the relation between volume and the ratio of observed to expected mortality for each hospital year of observation. A locally weighted regression scatterplot smoothing curve fitted to the data shows a relatively weak relation at high volumes but a much stronger effect at low volumes, especially those below 150 cases. These data suggest that concerns about the volume of coronary artery bypass grafting are primarily

Relation between volume of coronary artery bypass grafting and mortality adjusted for risk, California, 1983-9