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