400 mg, 800 mg, and 1200 mg groups were 87, 88, and 95, respectively, corresponding to death rates of 54%, 56%, and 61% ($p=0.65$, log rank test). Ten patients (2%) were lost to follow up.

On the basis of this and other randomised dose studies, in which the doses of the drug were 500 mg *v* 1500 mg² and 600 mg *v* 1200 mg,³ it may be concluded that to obtain the maximum effect on survival rates the dose of zidovudine need not exceed 400 mg daily.

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Management of septic shock

EDITOR,—I am grateful for the interest shown by C J Hinds and colleagues¹ in my review on management of septic shock.² The points raised concerning the use of inotropes are highly relevant to clinical management on the intensive care unit. I should like to clarify some issues.

Firstly, on the question of control of studies aimed at optimising levels of oxygen delivery, two of the three studies quoted did not have a concomitant control group, though one involved comparison with a well matched historical group treated with dopamine which had a mortality of 83%.^{3,4} The problems of control were highlighted by the third study, which was terminated on the advice of the hospital ethical committee because of a clear difference in survival between those treated to optimal oxygen delivery and those treated by a so called "normal protocol"—which in fact included the addition of dobutamine to standard vasopressor support to maintain a high normal cardiac output and therefore was not a true test of the hypothesis but may well have resulted in an even higher death rate in the control group without the additional inotropic support.⁵

The salient point for the practising clinician is that every published study of true septic shock requiring exogenous catecholamines for support of blood pressure between 1967 and 1989 (in which dopamine has been the mainstay of treatment) has shown mortality in excess of 70%. Where the effects of dopamine on cardiac output have been documented it has been shown to be unpredictable and in many cases undesirable. As stated in the review, an oxygen delivery of 600 ml/min/m² is not supranormal but normal—consistent with Hinds *et al*'s comments concerning maintenance of a normal cardiac output.

The potential dangers of inotropic and vasopressor treatment are emphasised on p 1663 of the article and were well aired after our original description of goal directed therapy in septic shock in subsequent correspondence. The paper quoted involved meticulous, painstaking, and tedious bedside manipulation and observation⁶; however, it is not totally relevant to management of septic shock as it was of a heterogeneous population of critically ill patients. The commonest cause of tachycardia in response to dobutamine at any dose is hypovolaemia, whatever the level of pulmonary wedge pressure. It is not stated in their study whether other agents such as phosphodiesterase

inhibitors were used when catecholamines failed, as recommended in the review. Not achieving appropriate values of cardiac output could signify an underlying lack of cardiac reserve, in which case the prognosis is grave. Another and equally strong possibility, however, is inadequately treated sepsis,⁷ which may sometimes be embarrassingly discovered at necropsy. Another pointer to this is persisting hyperlacticaemia despite apparently adequate levels of oxygen delivery. This is a much more practical problem, well reviewed recently, rather than unproved speculation concerning redistribution of blood flow caused by inotropic support.

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Teenagers, sex, and risk taking

EDITOR,—The article by Alan Mellanby and colleagues¹ prompts a few comments concerning teenagers' values and preferred ways of obtaining contraceptives which were shown by our study among a representative sample of 15-16 year old secondary school pupils ($n=516$, 266 boys) in a district in South Wales during spring term 1993.

A minority—14% (37) of boys and 4% (10) of girls—came under strong peer pressure to have sex, and the pressure was greater among boys than among girls. Thirteen per cent (34) of boys and 22% (56) of girls were already in a stable relationship and were likely to be sexually active.

When asked about obtaining contraceptives, most boys and girls preferred condom vending machines (table). The school nurse was not a popular choice. The important message that emerged was that the teenagers prefer anonymity when obtaining contraceptives.

Concern was raised by the Royal College of Obstetricians and Gynaecologists working party² on the basis of the findings of a study in the London borough of Brent which revealed that boys saw safe sex as the girls' responsibility.³ Our study showed that more than 90% (240) of Welsh boys and 96% (241) of the girls thought that both boys and girls were equally responsible for safe sex, contraception, and disease prevention. Most of them believed in one stable relationship (65% (174) of boys and 73% (183) of girls) and did not believe in casual sex (64% (172) and 81% (203)). Almost all the teenagers said unprotected sex could lead to sexually trans-

Preferred ways of obtaining contraceptives. Subjects responded yes or no to each option

	No (%) of boys ($n=266$)	No (%) of girls ($n=250$)
Condom vending machines	234 (88)	214 (85)
Free condoms in cinemas or discos	191 (72)	140 (56)
Over the counter in chemists	152 (57)	160 (64)
Special school nurse	117 (44)	118 (47)

mitted diseases and unintended pregnancies, and more than 90% of girls and boys indicated that condoms play a vital part in preventing pregnancy and sexually transmitted diseases.

It is obvious that the Welsh secondary school pupils' awareness and values are honourable. Their expressed need for anonymity while obtaining contraceptives should therefore be respected.

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Bronchodilator treatment in asthma

EDITOR,—M R Sears and D R Taylor note a difference in the proportion of deaths in young patients compared with the age mortality rate for asthma in the United Kingdom as a whole. They correctly note that the interpretation of these data depends on the demographics of the patients studied. This was clearly listed in table 1 in our paper. We plotted the age of distribution for patients who received salmeterol in our study on the graph of Sears and Taylor for comparison. This shows that the age distribution of those dying closely matched that of the study population. There is an important difference between the demographics of the patients in our study and the population of adults treated for asthma as the number of patients between 18 and 65 in our study was nearly 40% greater than expected. This difference explains the discrepancy noted by Sears and Taylor.

The number of patients dying in hospital is totally in line with epidemiological data in the United Kingdom given that one third of asthma deaths in Britain occur in hospital,^{2,3} which is more than the 25% which occurred in the salmeterol group.

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Management of trauma

EDITOR,—Recent reports in the press have stated that the experimental regional trauma centre set up by the Department of Health at the North Staffordshire Royal Infirmary is having considerable benefits on the outcome of major trauma.^{1,2} David Skinner has perhaps unintentionally reinforced that view by pointing out that the Department of Health is also funding a formal evaluation

of the trauma centre, and juxtaposing that fact with the statement that "early results are promising."

The department's evaluation, for which we are the principal investigators, does not show early results which are either promising or not promising. We have no early results. When data collection is complete in the middle of next year, but not before, we shall analyse the results to quantify the contribution of the trauma centre to the outcome of major trauma in the region.

We believe that the impression that the trauma centre is showing promising results is founded on the results put out by the trauma centre itself. Several points are worth bearing in mind, however. Firstly, the contribution of the trauma centre to the outcomes of trauma in the region depends on the proportion of patients with major trauma in the region who arrive at the trauma centre as well as on the performance of the centre itself. Secondly, improvements in outcomes may be taking place everywhere in the United Kingdom and therefore it is the relative improvement that matters. Thirdly, reports from outside the United States have not always favoured regionalisation of major trauma services.⁴ Most importantly, whatever benefits the trauma centre brings, these have to be set against the costs of the service to assess whether regionalisation may be justified.

The Department of Health's advisory group on health technology assessment strongly advised that new forms of care should not be offered within the NHS until their effects had been assessed.⁵ We hope that the community of people involved in trauma care will wait until our assessment is complete before making up their minds about the value of regional trauma systems in the United Kingdom.

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Termination of pregnancy with mifepristone

EDITOR,—The World Health Organisation Task Force on Post-ovulatory Methods of Fertility Regulation has evaluated the efficacy of various single doses of mifepristone followed by the prostaglandin analogue gemeprost in the indication early pregnancy termination.¹ The authors conclude that a single dose of 200 mg is as effective as 600 mg when used with gemeprost in pregnancies up to 56 days of amenorrhoea.

We would like to emphasise that a single dose of 600 mg is the only dose of mifepristone currently approved by regulatory authorities in those countries where mifepristone has been granted marketing authorisation.

The reason for the initial selection and Roussel's continued recommendation of a 600 mg dose is that early studies, using mifepristone alone for the termination of early pregnancy, showed a significantly higher rate of ongoing pregnancy with doses of 200 mg and 400 mg than with doses of 600 mg and 800 mg.²

Although mifepristone is now used with a prostaglandin analogue, the possibility that a woman will not reattend for administration of the prostaglandin analogue, despite thorough

counselling on the risk of possible teratogenesis, cannot be excluded.

There is no evidence that a 200 mg dose of mifepristone is better tolerated than a dose of 600 mg. The use of 600 mg, therefore, minimises the risk of ongoing pregnancy in women who do not receive the prostaglandin analogue, while not exposing the entire patient group to an increased risk of adverse effects.

In addition, the age of the pregnancy may be a critical factor in the rate of ongoing pregnancies. Therefore, it would not be prudent to extrapolate the results obtained in pregnancies of up to 56 days of amenorrhoea, as is the case in this study, to pregnancies up to 63 days, which is the maximum age of pregnancy for which mifepristone is currently licensed in the United Kingdom.

We strongly advise prescribers to continue to use only the licensed 600 mg dose of mifepristone in the indication of early pregnancy termination.

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The double contrast barium enema

EDITOR,—Siri Steine's paper on patients' experience of pain during double contrast barium enema examination will be helpful for general practitioners with an open access barium enema service available to them and also for the radiologists and radiographers performing the examinations.¹

The incidence of severe pain reported in the study is surprisingly low at 11% (252/2270) for a technique utilising room air as the insufflation gas.¹ The radiological literature suggests that patients experience severe² or "clinically relevant"³ pain more commonly with this examination technique; such pain was reported for 28/103 (27%) and 26/86 (30%) examinations, respectively. The reason for this discrepancy is that Steine's observations were restricted to pain occurring during the barium enema examination only, whereas the radiological series also recorded pain occurring after the patient had left the department. This omission seems sufficient to account for the much smaller proportion of patients reporting severe pain in the Norwegian series. In one of the radiological series 25 of the 35 patients who experienced severe pain responded to a follow up questionnaire regarding the pain.² Sixteen of these patients (64%) developed pain only after leaving the x ray department; most (13/16) experienced the onset of pain within one hour. It is obviously important to recognise that the onset of pain may be delayed in this way.

The same radiological papers also suggest that using carbon dioxide instead of air as the insufflation gas results in a significant reduction in the incidence of pain after enema. This is attributed to the more rapid rate of absorption of carbon dioxide from the bowel lumen. The use of carbon dioxide reduced the frequency of severe pain from 27% to 7% (95% confidence interval for difference 10% to 30%) and from 30% to 11% (7% to 32%). These papers argue strongly that changing the routine insufflation gas for barium enema examinations from air to carbon dioxide will dramatically reduce the total number of patients experiencing

severe pain after this common diagnostic investigation.

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How much alcohol is sensible?

EDITOR,—Geoffrey Smerdon does us all a service in asking for rationalisation of current guidance to the risks associated with different levels of alcohol consumption but does not go far enough.¹ A more important question than the consistency of the guidance is its validity.

The Royal Colleges of Physicians, General Practitioners, and Psychiatrists have all issued similar guidance on alcohol consumption, differing only in their variable and confusing use of "levels" and "limits" in the qualifying text. They have been coy about disclosing the scientific rationale for their recommendations (generally quoting "medical opinion"), but it seems to refer to the risk of hepatic cirrhosis, based largely on the findings of Pequinot and Tuyns, who studied a population of French people with cirrhosis of the liver.^{2,3} I do not question these findings (which were subject to all the difficulties associated with self reported consumption of alcohol), but the importance of the drinking pattern in the pathogenesis of cirrhosis and the differences existing in these patterns of drinking between Britain and France must reduce confidence in their applicability to a British population.

Current recommendations seem still to be based exclusively on health cost with no consideration for the evidence for health benefit, even in the narrowly physical sense (that is, disregarding intangible benefits such as pleasure and social wellbeing). The evidence for physical health benefit may not yet be firmly established, but this evidence is probably as reliable as the health cost evidence that underpins (so far as can be defined) the prescriptive recommendations of the royal colleges. It seems that evidence of harm rapidly becomes received wisdom, but evidence of benefit is challenged or disregarded. As current guidance has now been incorporated into *The Health of the Nation*, a political rather than a scientific document, it is likely to achieve "tablets of stone" status, which, on the evidence, seems unwarranted. An open reassessment of the risks of alcohol consumption reflecting the evidence for both cost and benefit is needed now.

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Seeing is believing

EDITOR,—One of Minerva's pictures related to the case of a 2 year old boy who swallowed a coin, which was seen in an anteroposterior neck radio-