7560 in 1995, these hospitals performed roughly half of all abortions and deliveries in Norway that year and served a similar proportion of the total population. There are no separate abortion clinics in Norway.

Figure 1 shows that the number of abortions had increased by 5% in January and by 11% in February this year compared with the previous year. For the two months combined the largest increase in one institution was 22%.

Fig 1—Number of legal abortions carried out in the nine largest gynaecological departments in Norway, January and February, 1995 and 1996

We consider that the findings reported here are probably representative of those for Norway as a whole. The downward trend in the number of legal abortions has been replaced by an increase of nearly 8% in the first two months of this year; this equals the reduction seen over the preceding five years.

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Depression in carers of elderly people living at home

EDITOR—We wish to respond to the letters¹ generated by our paper on psychiatric morbidity in carers.² R H Bird raises the interesting suggestion that carers of older people may be at risk of drinking excessively. Possibly because we do not work in a substance misuse service, our clinical impression is that alcohol misuse in this population of carers is rare. Bird is, however, correct in assuming that we did not ask about alcohol misuse in the prevalence study. The spouse carers of people with psychiatric disorders have now been interviewed in more detail as part of a follow up study; none admitted to excessive alcohol consumption, although some of the index cases did.

J M Eagles suggests that we have misrepresented his findings.³ Our point was that his study found that "Supporters of demented relatives showed no increase in psychiatric morbidity on the [general health questionnaire] when compared with the supporters of non-demented elderly." It is possible that our results differed partly because of the differences in settings. It still remains true that Eagles *et al* did not make a formal psychiatric diagnosis in the carers and that a

further possible explanation of the difference in findings between their study and ours lies in the method of ascertaining cases.

The interesting study by Orazio Zanetti and colleagues shows the importance of the characteristics of carers in determining vulnerability to depression; these findings can best be seen as complementary to our results in generating a multifactorial model of carers' vulnerability.

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Transdermal glyceryl trinitrate for dysmenorrhoea

Confidence intervals for glyceryl trinitrate do not suggest a significant effect

EDITOR—Effective treatments for dysmenorrhoea (combined oral contraceptives and non-steroidal anti-inflammatory drugs) are available, but, as R Pittrof and colleagues state, contraindications to non-steroidal anti-inflammatory drugs make them unsuitable in some patients.¹ The authors suggest, on the basis of a small clinical trial, that transdermal glyceryl trinitrate is a clinically useful alternative. They quote P values for different outcome measures (total pain score, $P = 0.059$; pain score on worst day, $P = 0.048$; total headache score and headache score on worst day, $P = 0.4$), which to us hardly suggest a clinically meaningful effect. More importantly, in their table of results none of the confidence intervals suggests a significant effect because the differences in the scores obtained during treatment with glyceryl trinitrate and with placebo range from negative to positive.

The contradictory conclusions drawn from the significance levels and the confidence intervals seem to stem from the use of non-parametric tests (for the P values) and parametric estimation of the confidence intervals. Given the emphasis in the *BMJ* and other journals recently on the use of confidence intervals rather than significance levels,^{2,3} we are surprised that Pittrof and colleagues' conclusions should have been allowed to stand.

A larger trial may well produce a more definitive answer, but on the basis of existing data we believe that the authors' assessment of the efficacy of glyceryl trinitrate is unduly optimistic. We would recommend paracetamol for patients who cannot tolerate non-steroidal anti-inflammatory drugs.

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Authors' reply

EDITOR—We fear that A Li Wan Po and R W Stones have missed the main point of our study. We recruited a small, highly selected group of women with severe dysmenorrhoea primarily to see whether a very small dose of transdermal glyceryl trinitrate had any effect on period pain. Using self score charts and standard statistical techniques, we showed an effect on period pain but not on other variables. In this context it is important to note that headache was included not as an outcome of treatment but as a potential side effect.

Readers vary in their preference for parametric and non-parametric tests, particularly when, as in our study, the scale of measurement is not straightforward. As we gave Wilcoxon P values and tabulated confidence intervals (here equivalent to parametric *t* tests) the concerns of both groups of readers are met with an economy of space. Different tests will yield slightly different results, which emphasises why one should not to be obsessed with $P = 0.05$ as a critical value or 95% confidence intervals that include or exclude 0. In this case, the results of both tests broadly agree and suggest that the treatment is worthy of further interest.

The magnitude of the response is largely irrelevant as we were primarily interested in investigating a pharmacological therapeutic mechanism. Hence our study has not proved clinical usefulness but has suggested a possible treatment; further studies of efficacy, dose, and safety are needed. As for the suggestion that women with dysmenorrhoea who cannot take non-steroidal anti-inflammatory drugs should take paracetamol—most gynaecologists know that women attending their clinics because of painful periods have tried everything already.

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Contamination of ampicillin was probably due to reuse of disposable stoppers

EDITOR—In July last year a small non-government organisation started to support a 40 bed paediatric unit in Afghanistan. Essential drugs were one of the items provided. These drugs were bought from pharmaceutical wholesalers in Pakistan and transported to Afghanistan. In November the medical staff of the unit suspected that excess deaths were associated with a batch of ampicillin for injection. The aluminum seal of the phials was intact, but the underlying rubber stoppers showed puncture marks.

A review of (imperfect) case notes showed eight unexpected deaths after the use of about 500 suspect phials. All of these children had shown sudden deterioration, resembling that occurring in septic shock, some hours after intravenous

injection of the suspect ampicillin. This batch of ampicillin was taken out of circulation immediately, and samples were sent for analysis in Europe. Chemical analysis confirmed the presence of ampicillin but also of high concentrations of *N*, *N*-dimethylanalin, a degradation product, and of another, unknown, substance.

Culture showed *Pseudomonas* spp and an unknown organism in the first two phials and *Bacillus* spp and an unknown organism in the second two phials. The laboratory suggested that, in view of the unevenness of the contamination, the route of entry could have been the perforated stoppers. The non-government organisation informed the relevant authorities.

The fact that the aluminum seals of the phials were normal while the rubber stoppers were perforated indicates that the rubber stoppers were not perforated after the manufacturing process. Thus stoppers that were already perforated were probably used in the manufacturing process. The most likely explanation is that these stoppers were second hand—in other words, disposable material had been reused. In the Indian subcontinent it is common (and dangerous) practice to collect used disposable syringes and needles from hospitals and to repack them and sell them as new—hopefully after proper cleaning and sterilisation.

As far as I know, reuse of disposable stoppers has not been described before, but it seems possible that it is a new, illegal, probably profitable, but certainly highly dangerous enterprise.

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Alcohol consumption and risk of coronary heart disease

Studies suggest that wine has additional effect to that of ethanol

EDITOR,—In their review of the reduction in the risk of coronary heart disease due to moderate alcohol consumption Eric B Rimm and colleagues interpret the available studies as supporting a beneficial effect of alcohol without any additional effect of the specific beverage consumed (beer, wine, or spirits).¹ We do not challenge the paradigm that ethanol itself possesses some cardioprotective properties. In the Copenhagen city heart study we also found a reduction in mortality associated with occasional intake of all three types of beverage.² But studies that do not take into account all three types of beverage are not suitable for addressing the question of whether there is an additional effect of beer, wine, or spirits.

Rimm and colleagues included in their review 10 prospective population studies, of which three did not analyse the effect of all three types of alcoholic beverage because consumption of one or two of them was negligible. In two other studies the analysis did not take into account the intake of the other types of beverage. Of the remaining five studies, four suggested a greater beneficial effect of wine, although with different methodological and statistical strength. In Rimm *et al*'s study, which found a stronger beneficial effect of spirits, 12.2% of the male health professionals studied reported a total alcohol intake of more than 2 drinks a day.³ A breakdown of the figures showed that the number of subjects who drank each type of beverage were small. The exact data are not given, but we are told that spirits were the beverage most frequently consumed, and the broad confidence intervals give a hint of the small number of subjects in the groups that drank beer and wine.¹

Thus the ecological and prospective cohort studies, as well as pertinent clinical studies,^{4,5} suggest that wine has an additional effect to that of ethanol in reducing the risk of coronary heart disease.

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Authors' reply

EDITOR,—Many of the prospective studies that we reviewed could not take into account all of the three main beverages containing alcohol (beer, wine, and spirits) because of the limited frequency of consumption of some of them. We do not agree with Mørtén Grønbaek and Thorkild I A Sørensen, however, that this should necessarily prevent them from being included in a review of the benefits of moderate alcohol consumption. In the multivariate analysis of type of beverage in the Copenhagen study the authors examined the association between wine consumption and total mortality, holding the effects of spirits and beer constant statistically.¹ However, in the Honolulu heart study, in which beer accounted for almost all of the alcohol consumed,² and in the Italian rural cohort study,³ in which only wine was consumed, the effects of other types of beverage were held constant implicitly.

Arguably, studies looking at only a single type of beverage may be more informative than those looking at many, since measurement of each beverage may contain error due to overreporting or underreporting or differential error due to differences in drinking patterns. The inverse association reported between moderate beer consumption and coronary heart disease in the Honolulu heart study (relative risk 0.57) was similar to the inverse association reported for wine in the Copenhagen city heart study (relative risk 0.47 (95% confidence interval 0.35 to 0.62) and for spirits in the study from eastern Finland (0.3 (0.1 to 0.7)).⁴

Grønbaek and Sørensen state that they do not challenge the paradigm that ethanol has some cardioprotective properties. In their study, however, 1-2 drinks of spirits a day increased the risk of death from coronary heart disease (1.16 (0.98 to 1.39)).¹ If the ethanol in spirits reduced the risk of coronary heart disease to a degree similar to that reported for beer consumption in their study (0.79 (0.68 to 0.91)) then some other, unknown, component of spirits must have been almost doubling the risk of death from coronary heart disease among men and women consuming 1-2 drinks a day. This seems unlikely since most other studies have reported a significant inverse association between moderate consumption of spirits and coronary heart disease.⁴ Therefore, differences in relative risks between types of beverage in the Copenhagen

study, and in many other studies, are more likely to have been due to differences in lifestyle characteristics, such as diet and drinking patterns, than to any additional substantial benefit from the non-ethanol components of a specific beverage.

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Association cannot be assumed to be causal

EDITOR,—The Royal College of Physicians has estimated that alcohol is responsible for 25 000 premature deaths every year.¹ Medical professionals need to be cautious about making pronouncements that might encourage people to drink more. Two recent papers in the *BMJ* that seem to provide evidence of a protective effect of alcohol in relation to ischaemic heart disease^{2,3} were widely reported in the national media; it may be assumed that the net effect will be to shift upwards the distribution of alcohol consumption in the population.

Neither study provides convincing evidence that alcohol protects against heart disease. Association cannot be assumed to be causal, but the authors of both articles make this assumption. Eric B Rimm and colleagues write that "a substantial portion of the benefit is from alcohol."² Hans Ole Hein and colleagues discuss attributable risk among men who abstained from alcohol; this term is appropriate only to a causal relation.³

There are reasons to doubt a causal relation. In Hein and colleagues' study non-drinkers were older than drinkers, which suggests a lower all cause mortality. Subsequent higher mortality might be attributable to age, which would have a non-linear relation with mortality and therefore be inadequately controlled for in the regression. The authors did not analyse data from the 1971 baseline, and mortality related to alcohol before 1986 may have biased the sample. The authors dismiss the possibility of "sick quitters" causing bias but do not consider a possible "sick non-starter" effect, whereby those prone to heart disease never started drinking. Given that 87% of the non-drinkers had never drunk, this was potentially a much larger source of bias.

Rimm and colleagues base their claim for a causal relation on inconsistent observational data. Of 12 ecological studies cited, seven show a significant beneficial effect of wine, two show a harmful effect of beer, and only one shows a beneficial effect of spirits and one a beneficial effect of beer. Of three case-control studies, only one shows all forms of alcohol to be protective;