

The simple risk score in our paper goes some way to achieving this. However, we agree that more powerful and more detailed models are required. We did include preliminary versions of such models in our paper (tables 5 and 6), but these need to be validated on independent datasets before they are used in practice. We are in the process of validating these models and developing more definitive models in collaboration with the North American Symptomatic Carotid Endarterectomy Trial (NASCET) group³ and the Veterans Administration (VA#309) trial group.⁴ Each of the risk factors cited by Hoefnagels will certainly be included in the modelling process.

The mean numbers needed to treat and numbers needed to harm that Hoefnagels reports may be a little confusing. First, the risks quoted (stroke and death at 3 years) are derived from patients with 80–99% stenosis and not 70–99% stenosis.⁵ Second, that the values are identical suggests, at first glance, that endarterectomy is of no overall benefit in patients with recently symptomatic 80–99% stenosis. This is not the case because the immediate risk of surgery (7% major stroke, number needed to harm therefore 100/7=14) is traded against the risk of major stroke in patients with 80–99% stenosis who were randomly assigned medical treatment. This risk was 26.5% at 3 years.

There are other numbers that can be derived from studies such as these: the number needed to neglect (the number of patients that it would be necessary not to treat for a stroke to occur on medical treatment only [just under four in this case]); and the number treated pointlessly (the number of patients who are treated who would have done well had they not been treated [100%–26.5% in this case, ie, three of four]). However, the profusion of these various summary statistics often serves more to confuse than to inform, and with the possible exception of number needed to treat, clinicians could probably manage without them. Even numbers needed to treat are somewhat over-simplistic and cannot necessarily be applied to populations other than those in which the trials were done.

*P M Rothwell, C P Warlow

*Department of Clinical Neurology, Radcliffe Infirmary, Oxford OX2 6HE, UK; and Department of Clinical Neurosciences, Western General Hospital, Edinburgh
(e-mail: peter.rothwell@clneuro.ox.ac.uk)

1 Rothwell PM. Generalisability of the results of large randomised clinical trials. *J Nephrol* 1997; **10**: 1–2.

2 Rothwell PM. Can overall results of clinical trials be applied to all patients? *Lancet* 1995; **345**: 1616–19.

3 North American Symptomatic Carotid Endarterectomy Trialists' Collaborative Group. The final result of the NASCET trial. *N Engl J Med* 1998; **339**: 1415–25.

4 Mayberg MR, Wilson E, Yatsu F, et al. Carotid endarterectomy and prevention of cerebral ischaemia in symptomatic carotid stenosis. *JAMA* 1991; **266**: 3289–94.

5 European Carotid Surgery Trialists' Collaborative Group. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998; **351**: 1379–87.

Death rate from use of ecstasy or heroin

Sir—Sheila Gore (Oct 9, p 1265)¹ raises some fascinating points that highlight the difficulties of estimating death rates in young people who use ecstasy or heroin. We suggest that the situation is even more complex.

First, what constitutes an ecstasy-related or heroin-related death, may be difficult to define from current statistics. A parallel may be drawn with the monitoring of mortality related to volatile-substances abuse carried out at our medical school,² for which a criterion for inclusion is: "Would the deceased still be alive if (s)he had not abused the volatile substance?" By this criterion, deaths from causes such as road traffic accidents are included if the death was secondary to intoxication with a volatile compound. This approach seems appropriate for classification of deaths from both ecstasy and heroin. In addition, the value of extra information recorded in part V of the coroner's certificate, used in the collation of death rates, will depend in some instances on whether a comprehensive analysis for abused substances has been done on behalf of the coroner.

Second, the estimates described by Gore are based on the assumption that the drugs purchased are what they are supposed to be, whereas the drugs may be of variable strength and purity.

Although most ecstasy users intend to purchase MDMA (methylenedioxy-methylamphetamine), a wide range of other compounds are found in tablets sold as ecstasy. These include other ring-substituted phenylethylamines (such as methylenedioxyethylamphetamine) and herbal mixtures (such as ephedra and Ma Huang), and some tablets may not even contain any active ingredient. Ecstasy tablets have been found to contain 4-methylthioamphetamine, which may be even more toxic than MDMA, and in Europe is to become subject to control measures and penalties.³ Thus, it is not clear whether the definition of ecstasy-related deaths is

based on the detection of MDMA (or its metabolites), or whether the detection of other compounds is also classed as ecstasy use. Clearly, we need to use more precise language, since ecstasy may cover a broad range of substances.

Thus, we cannot be certain which illegal drugs young people are exposed to, based on accounts by the user, or from the analysis of substances seized by law-enforcement agencies. The users are unlikely to have access to analytical data for the substances they have purchased, even if they rely on the findings of self-use kits based on the Marquis test.⁴ These kits give very limited information, even when used in an analytical laboratory. Furthermore, drugs seized by law-enforcement agencies may be a very biased sample and may not be timely, since results are published only for drugs currently controlled under the Misuse of Drugs Act, and these results are not made public until the completion of legal proceedings.

We have obtained objective information on the substances available to young people. We analysed tablets, capsules, powders, and herbal material voluntarily surrendered during searches made as a condition of entry to dance venues. The substances were placed into secure containers (amnesty bins), which were later collected and sealed by the police. Our pilot study has revealed new information on the availability of illicit drugs within the London area. We were able to integrate these findings rapidly into our CD-ROM database for the identification of solid dose formulations (TICTAC),⁵ which is available to both health-care and law-enforcement professionals.

We suggest not only that information on the frequency and pattern of use of drugs by young people should be recorded, but also information on the identity and purity of the actual substances they are purchasing should be collected whether or not the drugs are controlled by the Misuse of Drugs Act.

John D Ramsey, Atholl Johnston,
*David W Holt

Analytical Unit, St George's Hospital Medical School, London SW17 0RE, UK
(e-mail: d.holt@sghms.ac.uk)

1 Gore SM. Fatal uncertainty: death-rate from use of ecstasy or heroin. *Lancet* 1999; **354**: 1265–66.

2 Anderson HR, Macnair RS, Ramsey JD. Deaths from abuse of volatile substances: a national epidemiological study. *BMJ* 1985; **290**: 304–07.

3 Eur-Lex. Official Journal of the European Communities. L244. 1999; **42**: 1.

4 Moffat AC, ed. Clarke's isolation and identification of drugs, 2nd edn. London: Pharmaceutical Press, 1986: 139.

5 Ramsey J, ed. TICTAC version 4.4. Norwich: Stationery Office, 1999.

Sir—There can be little doubt that Sheila Gore¹ highlights a flaw in current methods of defining and recording drug-related deaths in the UK. Such figures are vital in planning judicial policy, treatment services, and most importantly, prevention strategy. However, to achieve the degree of accuracy that Gore suggests would require regular surveys of drug users, which is difficult and cost prohibitive.

The National Programme on Substance Abuse Deaths (NPSAD) was established in 1997 to monitor drug-related deaths in the UK. Our response is to report the cause of death ratio, looking at the number of drug-related deaths in specific categories (ie, 15–24-year-olds) and the drugs implicated in these deaths. This allows quick surveillance of the pattern of deaths over time. NPSAD receives data on drug-related deaths from coroners in England and Wales. Cases must meet one or more of the following criteria: one or more psychoactive substances directly implicated in the death; history of dependence or abuse of psychoactive drugs; or presence of controlled drug at necropsy.

To facilitate comparison with national and international databases, cause of death is re-coded by International Classification of Diseases (tenth revision) categories. Cases are reported by demographic characteristics, drugs implicated in death, whether they were prescribed drugs, associated risk for age, sex, and history of drug use. The programme reports regional differences and trends over time.

The most recent report, which covered the period July to December, 1998, showed 695 drug-related deaths reported by 96 coroners in England and Wales (131 were aged 15–24 years). Heroin was implicated in 60 deaths (52 men, eight women) and ecstasy in four (all men).

A method to obtain an accurate death rate is to study a defined population, such as addicts notified to the Home Office Addicts Index. A 27-year study of notified addicts² recorded 1104 drug-related deaths in 15–24-year-olds, giving an average annual rate of 3.2 per 1000 person-years in the last 10 years. A 20-year study of notified addicts aged 15–19 years showed that teenage addicts are 12 times more likely to die before age 20 years than non-addicts of the same age.³

NPSAD does not distinguish between first-time, sporadic, and regular drug use, and we acknowledge that this information would be useful. However, it is very difficult to distinguish, record, and monitor this type of data.

The role of a central specialist

register, suggested by Gore, is currently fulfilled by our programme, with substantial collaboration from the Home Office and coroners in England and Wales. The data compiled by NPSAD is used by drug action teams in informing policy development in accord with national strategy.⁴ The programme is being extended to Northern Ireland and Scotland.

*J Lind, A Oyefeso, M Pollard,

A Baldacchino, H Ghodse

Department of Addictive Behaviour and Psychological Medicine, St George's Hospital Medical School, London SW17 0RE, UK

- 1 Gore SM. Fatal uncertainty: death-rate from use of ecstasy or heroin. *Lancet* 1999; **354**: 1265–66.
- 2 Ghodse H, Oyefeso A, Kilpatrick B. Mortality of drug addicts in the United Kingdom 1967–1993. *Int J Epidemiol* 1998; **27**: 473–78.
- 3 Oyefeso A, Ghodse H, Clancy C, Corkery J, Goldfinch R. Drug abuse-related mortality: a study of teenage addicts over a 20-year period. *Soc Psychiatry Psychiatr Epidemiol* 1999; **34**: 437–41.
- 4 Cabinet Office. Tackling drugs to build a better Britain. London: Stationery Office, 1998.

Folic acid fortification

Sir—Jean Lawrence and colleagues¹ (Sept 11, p 915)¹ report that median serum folate has increased in the USA since the Food and Drug Administration (FDA) mandated the fortification of cereals and grains. We see a similar inverse trend in plasma homocysteine testing. Homocysteine is, in part, a functional marker of folate status²—as folate rises, homocysteine concentrations would be expected to decrease.

The clinical reference laboratory at our institution has tested between 1500 and 3000 plasma homocysteine specimens each month since September, 1997. Records before that time were difficult to collate because of software limitations in our laboratory information system. Specimens were received from throughout the USA. Plasma homocysteine was measured by high-

performance liquid chromatography with electrochemical detection.³

The figure shows all specimens tested between Sept 1, 1997, and Aug 31, 1999, in which sex was known and age was 30–59 years. A limited age distribution was selected because homocysteine tends to increase with age. Although the average value for women was lower, the same trend was seen when data were separated by sex (data not shown). The higher number of specimens in 1998 corresponds to the increased interest in homocysteine, and the decrease from 1998 is due to the availability of commercial kits suitable for hospital-based testing.

Over the 8-month period from September, 1997, to March, 1998, percentiles seem stable. From April, 1998, however, there was an apparent downward trend. As of August, 1999, the last month for which we have complete data, the trend seems to continue. This pattern follows a slightly different time course from that described for folate, namely an upward trend beginning in 1997.¹ There are several possible reasons for this apparent lag in homocysteine response. First, other factors that affect homocysteine, such as vitamins B₆ and B₁₂, and genetic influences, may confound the comparison. Second, the populations may be substantially different. Third, as a functional indicator of folate metabolism, homocysteine may simply require more time in which to register an effect. For whatever reason, our data suggests that plasma homocysteine concentrations are falling. Folate fortification of food is a likely explanation.

The specific goal of folate fortification is to decrease the rate of neural-tube defects (NTDs).² In the UK, supplementation has not decreased the NTD rate.⁴ Although the effect on NTD rates remains to be seen in the USA, fortification does seem to be having an effect on homocysteine. In terms of its effect on coronary heart disease, the benefits of decreasing homocysteine could be substantial. As Lawrence and

