Letters

Do neuroleptic drugs hasten cognitive decline in dementia?

Carriers of apolipoprotein E ε4 allele seem particularly susceptible to their effects

EDITOR—We agree with Rupert McShane and colleagues that there is evidence for an association between treatment with neuroleptic drugs and a more rapid cognitive decline in dementia, but we would also point out an additional association with the apolipoprotein ε4 allele.[1] We followed up 135 subjects from the Camberwell dementia case register.[2] The patients all fulfilled the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria for Alzheimer's disease and had an initial score on the mini mental state examination of ⩾5 points (to avoid floor effects) over one year. Throughout this period 23 took neuroleptics and 112 had no evidence of use of neuroleptics. Neither age; sex; initial score on the minimental state examination; nor previous evidence of hallucinations, persecutory ideation, aggression, or sleep disturbance had any significant relation with the rate of cognitive decline over this period. The subjects who took neuroleptics, however, had a greater rate of cognitive decline than those who did not (mean (SE) 6.2 (1.0) *v* 2.1 (0.4) points a year, $P < 0.0001$).

One hundred of these subjects consented to apolipoprotein E genotyping. The presence of the apolipoprotein E ε4 gene alone was not associated with a greater rate of cognitive decline (2.7 (0.6) *v* 2.1 (0.7) points a year, $P = 0.50$), which was in keeping with earlier findings.[3] A comparison of rates of cognitive decline by neuroleptic use according to the presence or absence of the apolipoprotein E ε4 allele showed that neuroleptic use was not associated with a greater rate of decline in the 41 subjects not carrying the allele (4.2 (2.4) *v* 1.8 (0.6) points a year, $P = 0.2$) but was associated with a markedly increased rate of decline in the 59 subjects carrying the allele (7.9 (1.2) *v* 1.9 (0.5) points a year, $P < 0.0001$). Thus in this study neuroleptics were associated with a greater rate of cognitive decline in subjects with Alzheimer's disease, and carriers of the apolipoprotein E ε4 allele seemed particularly susceptible to their effects.

An interaction of the apolipoprotein E ε4 allele with other risk factors in Alzheimer's disease has been reported elsewhere,[4] and these data thus further support the role of the allele in modifying individual susceptibility to environmental and now possibly iatrogenic risk factors.

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1 McShane R, Keene J, Gedling K, Fairburn C, Jacoby R, Hope T. Do neuroleptic drugs hasten cognitive decline in dementia? Prospective study with necropsy follow up. *BMJ* 1997;314:266-70. (25 January.)
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Trials must determine which neuroleptics are best in dementia

EDITOR—Rupert McShane and colleagues conclude that neuroleptic drugs may worsen already poor cognitive function.[1] If confirmed in controlled trials, this is indeed an important finding. In their study the neuroleptics used were haloperidol, chlorpromazine, promazine, or thioridazine. The authors mention the possibility that the anticholinergic effects of these neuroleptics may have been responsible for the observed cognitive decline. They seem to have missed the opportunity to explore this possibility by comparing haloperidol (a butyrophenone compound with few anticholinergic effects) with the three other neuroleptics, all of which are phenothiazines with important anticholinergic effects. The importance of the anticholinergic effects of these drugs cannot be dismissed.

The rationale for using anticholinesterase inhibitors to treat dementia is based on the cholinergic hypothesis of dementia.[2] The diminution in presynaptic cholinergic neurones and receptors has been correlated with severity of dementia in Alzheimer's disease. Furthermore, anticholinergic drugs are known to impair learning in both animals and normal human subjects.[3] Anticholinesterase inhibitors are now broadly accepted as being of small but important benefit in improving cognitive function or slowing cognitive decline in early dementia.

It is reasonable to suggest that compounds with marked central anticholinergic effects may be associated with a worsening of cognitive function and therefore that the type of neuroleptics used may be of major importance. As neuroleptics (and carbamazepine) are the only compounds that have been shown to be of significant benefit, we use more selective antipsychotics (sulpiride, haloperidol, risperidone) preferentially to treat psychotic symptoms in dementia.

Psychotic symptoms can present major management problems for carers, and in the absence of suitable alternatives the use of neuroleptics is unlikely to be completely replaced—even if there were sufficiently trained staff to implement psychological or behavioural interventions.

Trials are needed to clarify which, if any, of the various classes of neuroleptics and new antipsychotic preparations are best suited for use in dementia.

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1 McShane R, Keene J, Gedling K, Fairburn C, Jacoby R, Hope T. Do neuroleptic drugs hasten cognitive decline in dementia? Prospective study with necropsy follow up. *BMJ* 1997;314:266-70. (25 January.)
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Advice to authors

We receive more letters than we can publish: we can currently accept only about one third. We prefer short letters that relate to articles published within the past four weeks. We also publish some "out of the blue" letters, which usually relate to matters of public policy.

When deciding which letters to publish we favour originality, assertions supported by data or by citation, and a clear prose style. Letters should have fewer than 400 words (please give a word count) and no more than five references (including one to the BMJ article to which they relate); references should be in the Vancouver style. We welcome pictures.

Letters should be typed and signed by each author, and each author's current appointment and address should be stated. We encourage you to declare any conflict of interest. Please enclose a stamped addressed envelope if you would like to know whether your letter has been accepted or rejected.

We may post some letters submitted to us on the world wide web before we decide on publication in the paper version. We will assume that correspondents consent to this unless they specifically say no.

Letters will be edited and may be shortened.

Authors have not proved their argument

EDITOR—Rupert McShane and colleagues report finding worsened cognitive functioning in a group who had been prescribed neuroleptic drugs.[1] In concentrating solely on possible changes in cognitive functioning, they are addressing only a part of the question that needs to be asked.

When any drug treatment is prescribed, the benefits have to outweigh problems due to side effects for its use to be worthwhile. Worsening cognitive functioning could be such a side effect. This needs consideration, and the following questions need to be asked. Firstly, what was the indication for the prescription of neuroleptics? What was the drug of choice and the dose regimen? Secondly, did the neuroleptics achieve what was required? Was the level of distress of the patient—due to agitation, hallucinations, or delusions—reduced? Thirdly, did the use of neuroleptics mean that the patient could be maintained at home when in other circumstances he or she might require permanent care in some type of institution?

McShane and colleagues dismiss the possibility that the neuroleptics seemed to cause more rapid decline "because patients who were already on a steeper trajectory of cognitive decline were more likely to be prescribed them" and on the grounds that the point when patients started treatment with neuroleptics coincided with an increase in their rate of cognitive decline. This seems to be a circular argument.

In their key messages the authors state that neuroleptics "may cause more rapid decline in cognitive function" and later that their study "does not prove a causal relation." This is contradictory. Their study was not designed to show cause and effect, and the best that can be said from the study is that there is an association.

These data seem to be rather old, as the study was conducted "before substituted benzamides such as sulpiride were largely used in Britain for treating elderly people." This raises doubts about the relevance of the findings, as practice over the past 10 years has changed considerably and, recently, newer atypical neuroleptics (such as risperidone and olanzapine) have been used with increasing frequency. We are concerned that this paper may lead to a reluctance or refusal to prescribe such drugs despite their very real benefits in appropriate cases. We agree that care must be exercised in decisions on when, what, how much, and how long to prescribe.

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Authors' reply

EDITOR—We are pleased that C Holmes and colleagues have replicated our finding that patients with dementia who take neuroleptics decline more rapidly than those who do not. Their finding that the association is confined to those with the apolipoprotein E ε4 is important and deserves wide attention. It may prompt the suggestion that the apolipoprotein E status of patients with dementia should be established before they take neuroleptics. A detailed clinical cost-benefit analysis of neuroleptics in dementia and replication of the finding are both, however, essential before this should be further considered.

We support Robert Tobiansky and Martin Blanchard in their call for controlled trials of different classes of antipsychotics and agree with P W Bentham and colleagues that our findings may not apply to all classes of antipsychotic drugs. Unfortunately, we are unable to examine whether neuroleptics with anticholinergic side effects had a greater effect on cognitive function than those without because insufficient subjects were taking drugs without such side effects. We disagree with Bentham and colleagues' implication that traditional neuroleptics are so rarely prescribed as to make our results irrelevant to current practice, but we fully support their view that the benefits as well as the risks of neuroleptics need to be taken into account in decisions on whether to prescribe them.

We disagree that our interpretation of the data is circular. The association we reported between more rapid decline and use of neuroleptics has three possible interpretations. Firstly, there may be a causal link. Secondly, it is theoretically possible that neuroleptics were prescribed not, as one might expect, for behavioural problems (which we controlled for in the regression analysis) but because the patients were declining faster. Our finding that the point of onset of more rapid decline coincided with the start of treatment makes this explanation improbable. A third possibility remains that neuroleptics were prescribed for reasons that were associated with more rapid decline but were not included in the regression analysis. We ruled out one such possibility, Lewy body disease, but there may have been others.

We did indeed state that neuroleptics "may cause more rapid decline in cognitive function" and also that our study "does not prove a causal relation." This is caution, not contradiction.

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Intake of micronutrients in Britain's poorest fifth has declined

EDITOR—The *Rome Declaration on World Food Security*, adopted on 13 November 1996, affirms the "right of everyone to have access to safe and nutritious food, consistent with the right to adequate food and the fundamental right of everyone to be free from hunger."[1] Hunger and inadequate food intakes are not confined to developing countries; poor people in Britain have also experienced a decline in food security over the past decade. The report *Low Income, Food, Nutrition and Health: Strategies for Improvement*, recently published by the Department of Health, documents the evidence.

Those on the lowest incomes, whether from means tested benefits such as income support or from low or insecure wages, have markedly low micronutrient intakes. Since 1980, household intake of antioxidants among the poorest fifth of families in the United Kingdom has declined dramatically (β carotene by 47% and vitamin C by 23%).[2] The gap in fruit consumption between the rich and poor sections of the population is widening, reversing a trend from 1899.[3] Parents regularly go hungry to pay domestic bills or ensure children are fed[4]; micronutrient intakes are so low as to jeopardise health in households where income support is reduced to recoup fuel, rent, or water debts (20% of claimants).[5]

The world food summit highlighted poverty as the major cause of food insecurity: this is true for Britain too. One in 20 teenagers experiences homelessness and is reliant on day centres or "soup runs" for basic needs. One in four households in the United Kingdom lives on less than £115 a week. Low income households lack access to an affordable nutritious diet: they have insufficient money and often live on estates devoid of shops. The rise in superstores at the expense of markets and small shops is well documented: Kwik Save, a major discount store serving poor communities, last year announced closure of 10% of its stores to survive in the highly competitive food market.

The Department of Health report called for a coordinated national policy for food and low income, and better support for local initiatives. The latter are easy targets for cuts in all sectors; the food needs of poor people are seldom on the political agenda. The British government accepted the high minded objectives in the Rome declaration: "Governments will implement cost-effective public works programmes for the unemployed, [and] develop social welfare and nutrition safety nets to meet the needs of the food insecure." There is still a long way to go.

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1 *Rome declaration on world food security and world food summit plan of action. World Food Summit Rome 13-17th November*

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More women drink at hazardous levels in England than Italy

EDITOR—Marco Piccinelli and colleagues describe 482 patients who presented to 10 primary care clinics in Italy and completed the alcohol use disorders identification test.[1 2] In England we are conducting a randomised controlled trial of methods to encourage the uptake and use by general practitioners of a brief alcohol intervention programme incorporating the alcohol use disorders identification test as its screening questionnaire. We have compared characteristics and drinking behaviour of primary care patients in Italy and England.

In our study 128 general practitioners from northern England (one per practice) agreed to implement a brief intervention programme. They were asked to screen the alcohol consumption of all patients over 16 who attended their surgery and to give advice plus a booklet to hazardous drinkers. Data have been analysed for 31 general practitioners (data from 4746 questionnaires completed by patients).

Figure 1 shows characteristics of the patients presenting in Italy and England. Although there was no age limit in England, the two samples were relatively comparable. Piccinelli and colleagues diagnosed hazardous drinkers on the basis of quantity-frequency criteria and harmful drinkers on the basis of criteria in the 10th revision of the *International Classification of Diseases.* We defined hazardous drinkers as those scoring 8-12 on the questionnaire for the alcohol use disorders identification test and harmful drinkers as those scoring 13 or more. In Italy 62 (12.9% of the sample) were hazardous drinkers, of whom 11 (17.7%) were women; and 15 (3.1%) were harmful drinkers, of whom 2 (13.3%) were women. In England sex was identified for 4716 (99.4%) of the patients. Of this sample, 713 (15.1%) were hazardous drinkers, of whom 304 (42.6%) were women; and 191 (4.1%) were harmful drinkers, of whom 70 (36.6%) were women.

The proportion of women in the categories of hazardous and harmful drinking was much higher in England than Italy. The different ways in which hazardous and harmful consumptions were defined between the studies may have affected these findings but are unlikely to have accounted for such large discrepancies. The greater number of English women drinking excessively may reflect different cultural acceptance of drinking by women in Italy and in England. In England the proportion of women drinking hazardously has increased, from 9% in 1984 to 13% in 1994, while men's drinking has remained stable over this time.[3] Our findings suggest that excess drinking by English women is an important issue that should be specifically addressed if we are to meet the targets for alcohol in the Health of the Nation. Given that a high proportion of women present to primary care,[4] this seems to be the ideal setting for such work.

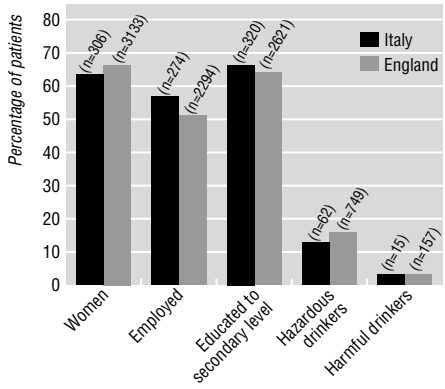

Fig 1 Demographic characteristics of patients presenting to primary care and completing questionnaire for alcohol use disorders identification test in Italy and England (mean age 42.2 (SD 14.4) years in Italy and 46.7 (17.7) years in England; age range 18-65 in Italy and 16-96 in England)

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1 Piccinelli M, Tessari E, Bortolomasi M, Piasere O, Semenzin M, Garzotto N, *et al.* Efficacy of the alcohol use disorders identification test as a screening tool for hazardous alcohol intake and related disorders in primary care: a validity study. *BMJ* 1997;314:420-4. (8 February.)
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Prophylaxis should be considered even for trivial animal bites

EDITOR—In their report of a case of purpura fulminans caused by infection with *Capnocytophaga canimorsus* after a dog bite, D J Mellor and colleagues suggested that *Pasteurella* spp, *Staphylococcus aureus*, and anaerobic organisms were susceptible to erythromycin and tetracycline.[1] Unfortunately, as few as 20% of *Pasteurella multocida* in wounds may be sensitive to erythromycin,[2] and *P multocida* meningitis has been reported after failure of treatment with erythromycin.[3]

In cat bites, in which the risk of pasteurella and anaerobic infection is dramatically increased, neither tetracycline nor erythromycin provides sufficient cover.[3 4]

Bites from other domestic animals including pigs and horses are not uncommon in our largely rural population, and we have also encountered bites from adders, monkeys, and even a cockatoo. For prophylaxis against infections from large pig bite wounds I advocate adding ciprofloxacin to co-amoxiclav so that any Gram negative organisms such as *Flavobacterium* species group IIb will be covered. Empirical ciprofloxacin would provide cover against species of *Vibrio*, *Aeromonas*, and *Pseudomonas* and should be considered after bites from exotic pets such as reptiles and marine animals.

As 32% of all cases of *C canimorsus* septicaemia to date have occurred in asplenic patients,[5] we routinely tell such patients to seek urgent medical attention and antibiotic prophylaxis for even the most trivial of animal bites.

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1 Mellor DJ, Bhandari S, Kerr K, Bodenham AR. Man's best friend: life threatening sepsis after minor dog bite. *BMJ* 1996;314:129-30. (11 January.)
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Giving children adults' rights runs risk of making them adults before their time

EDITOR—Gerison Lansdown and colleagues' editorial on implementing the UN Convention on the Rights of the Child is remarkable for failing to mention the word "parent" even once.[1] If national and international government policy is ever to address the needs of today's children it must recognise that one of the primary rights of every child should be adequate parenting. Without this any child is at an immediate and probably permanent disadvantage. Thus, surely, any policy involving children must be formulated on the basis of the effects it is likely, or intended, to have on the parenting process. Policies that leave parents with less time, energy, or financial resources for their children are not in the interest of the children—or, indeed, of society as a whole.

The editorial seems to assume that if a set of predominantly adult rights is ascribed to children then those children will somehow automatically develop into responsible adults, without any other input. The authors

are rightly concerned about the question of reasonable chastisement but offer no guidance on any workable alternatives in setting limits to behaviour. By treating children as adults in the definition of their rights we run a risk of making them adults before their time. Perhaps, then, we should not be surprised when they turn up in court facing charges usually associated only with adults, such as murder.

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1 Lansdown G, Waterston T, Baum D. Implementing the UN Convention on the Rights of the Child. *BMJ* 1996;313:1565-6. (21-28 December.)

Hypoplastic left heart syndrome

More families now have a choice

EDITOR—We support the assertion by O'Kelly and Bove in their editorial on hypoplastic left heart syndrome.[1] Over the past four years our unit has performed over 100 Norwood procedures for this condition, of which 37 were in 1996. The referral pattern suggests that more families are being given the choice in the United Kingdom. We share O'Kelly and Bove's positive encouragement stance for these patients, backed by a dedicated team rather than offering terminal care. Transplantation is not an alternative practical option at present.[2]

Though most patients present soon after birth, an increasing number are diagnosed antenatally. Diagnosis in fetal life gives the opportunity for choice, counselling as well as planned delivery with service providers alerted. For some patients the course after the first stage can be slow and complicated with immense pressure on the parents and the rest of the family. Family support from the institutions carrying out this procedure is essential, but other parents can also provide valuable advice and help. To achieve this a national parent group has been set up, known as "Left Heart Matters," in order to support fellow parents with individual requests but also to organise an annual get together; an information booklet for parents has also recently been published by this group. Information on Left Heart Matters and the booklet can be obtained from: Suzie Hutchinson, Cardiac Liaison Sister, Birmingham Children's Hospital, Ladywood Middleway, Birmingham B16 8ET.

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1 O'Kelly SW, Bove EL. Hypoplastic left heart syndrome: terminal care is not the only option. *BMJ* 1997;314:87-8.
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Willingness to initiate treatment is crucial

EDITOR—Sean O'Kelly and Edward Bove state that in the United Kingdom most children born with the hypoplastic left heart syndrome will be managed with supportive terminal care. In addition, they suggest that in general there has been "little interest" in surgical palliation of the syndrome in Britain.[1] We challenge these assertions.

At Guy's Hospital, London, after discussion between all relevant subspecialties, a programme of staged surgical palliation for hypoplastic left heart syndrome was begun in 1995. Eighty seven cases of the syndrome were diagnosed prenatally by fetal echocardiography during 1995 and 1996. All parents were counselled about the treatment options, and 38 sets of parents (44%) elected to continue with the pregnancy. There were five intrauterine deaths, and four pregnancies were ongoing. Of the 29 babies who were delivered, surgery was declined by the parents in six cases, and two babies died preoperatively. Twenty one babies underwent Norwood palliative surgery. In addition, five babies who were diagnosed postnatally also had surgery. Of this total group of 26 babies, there were 14 survivors (54%), of whom six subsequently survived stage 2 of the Norwood protocol with no deaths during the second stage. Of the first 13 babies, four survived, but 10 of the last 13 survived initial palliation, suggesting that with experience results have improved.

Most of our cases were diagnosed prenatally, and the number of parents who opted for termination or declined intervention postnatally suggests that many are not prepared to put their child through multiple operations with an uncertain long term outlook. We entirely agree with O'Kelly and Bove that the willingness of a unit to initiate a treatment strategy is crucial, particularly in the early stages, and think that our recent results justify our efforts. The results of postnatal treatment seem to be improving, and there is reason for cautious optimism that this trend will continue.

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1 O'Kelly SW, Bove EL. Hypoplastic left heart syndrome: terminal care is not the only option. *BMJ* 1997;314:87-8.

Quality of life is also important

EDITOR—Sean O'Kelly and Edward Bove suggest that we should adopt more active management of babies with hypoplastic left heart syndrome in Britain.[1] Bill Brawn's results in Birmingham over the past four years are commendable but he expresses caution about the long term outcome for these babies.[2]

Surgery and the postoperative period are extremely difficult. Survival is important but so is quality of life. Very little has been published on neurodevelopmental outcome. One recent small follow up study from New York, however, reported that of 11 survivors, four had moderate and three severe to profound mental retardation when assessed at 11-67 months of age.[3] Delayed motor development was seen in five children and cerebral palsy in two.

Palliative surgery is increasingly available for hypoplastic left heart syndrome in Britain, though surgery is still less common than in the United States. The alternative active management option of transplantation will remain constrained by a severe shortage of donor hearts.

I urge that children who survive the three stage Norwood palliation of hypoplastic left heart syndrome should have detailed neurodevelopmental follow up to ensure that they receive the necessary input for any developmental problems which become apparent and that units undertaking such surgery should carefully audit and publish quality of life outcome rather than just survival. If the neurodevelopmental outcomes are as poor in Britain as they are in the United States my view would be that parents should be very carefully counselled about treatment options, which should include offering terminal care only.

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1 O'Kelly SW, Bove EL. Hypoplastic left heart syndrome: terminal care is not the only option. *BMJ* 1997;314:87-8.
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National system for monitoring all drug use in pregnancy already exists

EDITOR—Discussion of the postmarketing surveillance of a new epileptic drug caused John J Craig and James I Morrow to report their establishment of a register of epileptic patients who become pregnant.[1] This is a worthy venture, but doctors may become confused about where they should send communications on drug outcomes in pregnancy.

The National Teratology Information Service is a unit in Newcastle upon Tyne, funded by the Department of Health; it both provides information on drug use in pregnancy and monitors the outcome of pregnancy for a range of drugs, including anticonvulsants. The centre is also part of a European network of teratology information services, which enables the pooling of data from across the European Community and hence has the potential to produce a more comprehensive comparison of risk.[2] In addition, obstetricians in Scotland have their own initiative in collaboration with us.

In these circumstances, therefore, we wish to remind readers of the national system, which applies to all drug use and chemical use in pregnancy of which we are

notified. We hope that Craig and Morrow will collaborate with existing national databases, including that held by the Committee on Safety of Medicines, which is used extensively for drug regulatory purposes.

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1 Craig JJ, Morrow JI. New antiepileptic drugs. *BMJ* 1997;314:603. (22 February.)
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Hormone replacement therapy

Damage is done by pressure groups that distort the evidence

EDITOR—Elizabeth H Price and colleagues present a biased analysis in their letter stating that women need to be warned about the dangers of hormone replacement therapy.[1] They confuse the epidemiology of oral contraceptive use and that of hormone replacement therapy, which is less advanced. They claim an increased incidence of ovarian cancer with oral contraceptives (wrongly described as contraceptive hormones). It has been known for 20 years that they protect against ovarian cancer.[2] The magnitude is important and long lasting and increases with duration of use. They make the same claim for "menopausal hormones." It is not true of unopposed oestrogen (they selected one of six papers). It is obviously untrue for combined oestrogen-progestogen therapy.

They omit any reference to the protective effect of the pill against endometrial cancer (the benefit is similar to that seen with ovarian cancer). They misrepresent the situation with regard to osteoporosis: only the duration, not the existence, of benefit has been questioned. They exaggerate the effect on breast cancer by selective citation. Price and Little were accused of doing this after a similar biased letter last year.[3] They ignore the better balanced analysis by Beral *et al*.[4] They suppress the information on reduced tumour spread in oral contraceptive users. Such a catalogue of false information, misrepresentation, and suppression of inconvenient evidence is sadly, and increasingly, a characteristic of many pressure groups.

Similar activities have often caused major harm to the groups they purported to help. Ill informed attacks on safe intrauterine devices after the withdrawal of the Dalkon Shield, which was unsafe, led to the abandonment of Lippes loops and Copper T devices by the Population Council and also of the Copper 7, which was the only device suitable for nulliparous women. Many women throughout the world suffered as a result. Attacks on Debendox (bendectin) led to its withdrawal despite the positive support of regulatory agencies. Similar lobbying against pertussis vaccine led to a decline in its use and to children dying of whooping cough. I have reviewed elsewhere the adverse impact of the AIDS lobby on patients.[5]

The above examples show the damage that can be done by pressure groups and single issue fanatics who distort the evidence. Lobbying against the pill in the 1970s led to a disastrous decline in the funding of research into improved contraceptives, which set back progress by several decades. Women need truthful, accurate, and fair information on the risks and the benefits of hormonal steroids. They need protection from misrepresentation by DASH.

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1 Price EH, Little HK, Grant ECG, Steel CM. Women need to be warned about dangers of hormone replacement therapy. *BMJ* 1997;314:376-7. (1 February.)
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Be cautious about using HRT for women without symptoms of oestrogen deficiency

EDITOR—Elizabeth H Price and colleagues express doubts about the beneficial effects of hormone replacement therapy in preventing cardiovascular diseases and osteoporosis.[1] This is quite remarkable because there is sometimes on the one hand a tendency to understate the possible risks of hormone replacement therapy (particularly the risk of breast cancer), while on the other hand the assumed protective effects are overemphasised, especially by those who take the menopause as an adverse event.[2 3]

The doubts can be supported by a review of those studies that are regarded as efficacy proofs of hormone replacement therapy concerning the prevention of hip fractures, which are the most important manifestation of osteoporosis. The review included studies published until 1995 (table 1); from multiple publications of the same study only the latest was included.[4]

There is an inverse relation between the protective effect seen in the analysed observational studies and the methodical state of the respective types of study. The odds ratios found in case-control studies ($n_1 = 7$) varied from 0.22 to 0.72 for ever users compared with non-users of hormone replacement therapy, indicating a substantial preventive effect; while there was a range of 0.65 to 0.85 in retrospective ($n_2 = 3$) and a range of 0.79 to 1.02 in prospective ($n_3 = 3$) cohort studies, respectively, indicating only a slight or no effect. The type of study (case-control, retrospective, or prospective cohort) explains about 63% of the variability in the relative risk estimators; the difference between the three types of studies is significant (analysis of variance, $P < 0.01$, $F = 8.59$, 2 df).

On the basis of these findings, until the results of the first randomised study primarily investigating the protective ability and detrimental effects of hormone replacement therapy are available, one should be cautious about suggesting the use of hormone replacement therapy for women without symptoms of oestrogen deficiency.[5] At the very least, the women should be informed about the background of both the risks and benefits.

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1 Price EH, Little HK, Grant ECG, Steel CM. Women need to be warned about dangers of hormone replacement therapy. *BMJ* 1997;14:376-7. (1 February.)
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Table 1 Results of studies regarding hormone replacement therapy (HRT) and the prevention of hip fractures (ever users *v* non-users)

Study	Type	Odds ratio/relative risk (95% CI)	Reference
Hutchinson *et al*, 1979	CC	0.22 (0.06 to 0.81)*	*Lancet* 1979;ii:705-9
Weiss *et al*, 1980	CC	0.48 (0.36 to 0.63)*	*N Engl J Med* 1980;303:1195-8
Johnson and Specht, 1981	CC	0.72 (0.48 to 1.09)	*Am J Public Health* 1981;71:138-44
Paganini-Hill *et al*, 1981	CC	0.72 (0.42 to 1.22)*	*Ann Intern Med* 1981;95:28-31
Kreiger *et al*, 1982	CC	0.48 (0.27 to 0.86)	*Am J Epidemiol* 1982;116:141-8
Kanis *et al*, 1992	CC	0.55 (0.36 to 0.85)	*BMJ* 1992;305:1124-8
Grisso *et al*, 1994	CC	0.48 (0.19 to 1.25)*	*N Engl J Med* 1994;330:1555-9
Kiel *et al*, 1987	RC	0.65 (0.44 to 0.98)	*N Engl J Med* 1987;317:1169-74
Looker *et al*, 1993	RC	0.89 (0.52 to 1.50)	*Osteoporosis Int* 1993;3:177-84
Maxim *et al*, 1995	RC	0.85 (0.41 to 1.80)	*Osteoporosis Int* 1995;5:23-9
Naessen *et al*, 1990	PC	0.79 (0.68 to 0.93)	*Ann Intern Med* 1990;113:95-103
Paganini-Hill *et al*, 1991	PC	1.02 (0.81 to 1.27)	*Epidemiology* 1991;2:16-25
Cummings *et al*, 1995	PC	1.00 (0.60 to 1.50)	*Engl J Med* 1995;332 767-73

CC=Case-control. RC=Retrospective cohort. PC=Prospective cohort. *Own calculations based on published data.

Studies exploring health in relation to intrauterine life should look at birth order

EDITOR—Stephanie J C Taylor and colleagues report a cross sectional study of size at birth and blood pressure.[1] We would underline the fact that birth order is not taken into account in most studies exploring health in relation to size at birth. Yet birth order is the best known single factor influencing birth weight and placental ratio. For example, according to a British calculation, the average difference in birth weight between firstborn and secondborn children is 138 g.[2]

One of us (JT) has assessed the levels of anxiety of male and female students aged 20 by using the "STAT test." A significant positive correlation between levels of anxiety and birth weight was originally presented as the main conclusion of the study.[3] Afterwards we controlled for birth order. It now seems that one of the main factors influencing anxiety levels at age 20 is birth order.

Most epidemiological studies exploring health in relation to intrauterine life have largely ignored birth order; studies that focus on birth order are conducted in the framework of social sciences and tend to ignore fetal life. Interdisciplinary bridges need to be built.

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1 Taylor SJC, Whincup PH, Cook DG, Papacosta O, Walker M. Size at birth and blood pressure: cross sectional study in 8-11 year old children. *BMJ* 1997;314:475-80. (15 February.)
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Dictating clinic letters in front of the patient

Letting patients see copy of consultant's letter is being studied in trial

EDITOR—B W Lloyd shows that patients approve of a consultant's dictating clinic letters in front of them, but Mike Pringle asks for more evidence to support the idea.[1] Our study, funded by Devon Family Health Services Authority, may give this evidence.

During 1994, consecutive referrals from two general practitioners were randomised to (*a*) dictation in their presence or immediately after they left the room and (*b*) whether they were sent a copy of their referral letter. Terminations of pregnancy were excluded. All patients were sent a questionnaire. We monitored attendances at hospital.

Altogether 171 patients entered the study. The randomisation was to a Latin square design. Thus, of the 137 (80%) patients who responded to the questionnaire, 65 had had dictation in their presence and 72 had not; and 70 had received a copy of the letter and 67 had not. Forty patients received both dictation and a copy of the letter. Fifty three patients rated dictation in their presence very helpful, nine moderately helpful, and two not very helpful; one patient made no answer. Fifty three patients rated receipt of a copy letter very helpful, 12 moderately helpful, and five not very helpful. Eighty one respondents stated that the referral process had increased their understanding of their condition. This was unrelated to dictation in their presence or receipt of a copy letter.

Table 1 Accuracy of referral letter, depending on whether dictation was done in patient's presence, for patients who received copy of their referral letter. Figures are numbers (percentages)

Accuracy	Dictation in patient's presence	No dictation in patient's presence	Total
Completely accurate	31 (78)	13 (43)	44 (63)
Mostly accurate	6 (15)	12 (40)	18 (26)
Partly accurate	3 (8)	5 (17)	8 (11)

χ^2=8.61, P=0.013.

Table 1 shows the effect of dictating the letter in their presence on its accuracy, as judged by the patient. All 89 patients who received a copy letter attended their outpatient appointment, but five of the 82 without a copy letter did not attend.

Previous studies of sending a copy of hospital letters to the patient have shown 91-96% satisfaction among patients.[2 3] Lloyd's study and ours are as convincing for dictation. Immediate dictation or receipt of a copy letter relieves anxiety that the referral might be delayed. Equally plausible is that the new process includes the patient. One comment—"I feel I have been fully consulted and treated as an intelligent adult"—exemplifies this.

Assessments of the accuracy of referral letters, finding levels of 63-95%, have concentrated on measurable items, such as the presence of a drug history.[4] Thus our figure of 78% (31/40) complete accuracy after dictation in front of the patient cannot be directly compared but is much better than 43% (13/30) without immediate dictation.

The 100% attendance rate of those who received a copy letter and the 6% non-attendance rate of the controls, compared with a local mean non-attendance rate of 6.2%, is currently being studied in a randomised controlled trial.

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1 Lloyd BW. A randomised controlled trial of dictating the clinic letter in front of the patient. *BMJ* 1997;314:347-8. [With commentary by M Pringle.] (1 February.)
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Further research should be qualitative

EDITOR—In Editor's Choice the editor asks readers to take up the challenge of the methodology in B W Lloyd's paper.[1] I wonder whether we are asking the right question. Surely there is no doubt that patients (in this case parents) want and are entitled to full information about the consultation, and we as doctors should examine the process of how to provide this. It has already been established that parents appreciate receiving a copy of the letter to the general practitioner after an outpatient visit.[2 3] Yet it is still the exception for parents to receive such a letter, at any rate in my district. There are many questions about Lloyd's practice that a questionnaire would not answer: what happens if the parents disagree with the consultant's remarks? Is there an opportunity to question the consultant? What happens if there is something in the letter that the parents don't understand? What is the child's view of the dictated letter?

Mike Pringle's commentary is wrong to focus on the narrow issues of case mix and the phrasing of the questionnaire. Rather we should be examining why practice such as Lloyd's has not become the norm. Further research is indeed needed, but it should be qualitative and should examine the process of information giving from the parent's perspective, with the aim of making it truly interactive. This is a good example of a situation in which the priority is to put the existing research into practice rather than initiate yet further studies on the same question.

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1 Lloyd BW. A randomised controlled trial of dictating the clinic letter in front of the patient. *BMJ* 1997;314:347-8. [With commentary by M Pringle.] (1 February.)
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Effect of sending clients a personalised summary letter is being studied

EDITOR—B W Lloyd reports a randomised controlled trial of dictating the clinic letter in front of the patient. In his commentary Mike Pringle raises the issue of the settings in which it is appropriate to share clinic letters.[1] We are involved in a continuing study in psychiatric patients that is based on the philosophy that more open consultations are beneficial to patients. During the initial consultation with consecutive new outpatients we use a brief motivational interviewing approach and then send the client a personalised summary letter, detailing his or her problems, life story, diagnosis, and treatment. We do not dictate the letter in front of the patient, but a copy of the letter to the patient replaces the standard letter to the referring doctor and takes no longer to dictate. Matched control subjects drawn from two neighbouring teams receive only a standard psychiatric assessment only without a feedback letter.

So far, 56 patients and controls have been recruited. An independent researcher

Table 1 Patients' response to personalised summary letter sent to them

	No of patients
Very pleased	11
Quite pleased	9
Mixed feelings	5
Indifferent	2
Not very pleased	0
Not at all pleased	1

conducts a semistructured interview with the patient within a few weeks of the initial consultation, assessing satisfaction with various aspects of the consultation and compliance with treatment.[2] Most of the patients in the group who received a letter showed a positive response to receiving it (table 1). They often commented that it seemed personal, made them feel listened to and understood, and acted as a reference. Twenty six of the 28 patients reported that they found the letter easy to understand, and the same number considered the letter to be very or quite accurate. In the control group, 18 of the 28 patients said that they would have liked to receive a similar letter. Most importantly, there was also a trend for patients in the experimental group to be more satisfied with their initial consultation than the control subjects (Wilcoxon's matched pairs signed ranks test, $P = 0.07$).

Our preliminary findings suggest that it is feasible to share clinical information with patients in such a sensitive specialty as psychiatry and that this may positively affect patients' views of the consultation. We are now looking at the effect of the intervention on compliance with treatment and outcome, which we will report when the project is completed.

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1 Lloyd BW. A randomised controlled trial of dictating the clinic letter in front of the patient. *BMJ* 1997;314:347-8. [With commentary by M Pringle.] (1 February.)
2 Asch R, Price J, Hawks G. Psychiatric out-patients' reactions to summary letters of their consultations. *Br J Med Psychol* 1991;64:3-9.

Increasing doctors' confidence would solve low uptake of prehospital thrombolysis

EDITOR—Luke Vale and colleagues calculate that the additional cost of thrombolysis in the community compared with hospital use is modest and suggest further research on the impact of a policy of community thrombolysis.[1]

I work in a rural practice 35 km from the nearest district general hospital; anistreplase was introduced into the practice four years ago. The 10 doctors serve a resident population of 14 000 people; in addition there are many holidaymakers and a local community hospital. Almost all patients with chest pain are seen by a doctor before their transfer to the district general hospital. The practice has had an electrocardiograph and defibrillator for many years.

Prehospital thrombolysis has been used for four patients: anistreplase has been given once at home, twice in the surgery, and once in the community hospital. During the same period over 90 patients with a myocardial infarct were admitted to the district general hospital. In the light of Vale and colleagues' paper I asked the doctors why our use of anistreplase was so low. All the doctors were aware of the availability of anistreplase and that early thrombolysis is beneficial. Five doctors thought that the benefit was large (>10%), two thought it moderate, one thought it small (<5%), and one did not know. Three doctors had used anistreplase; interestingly, these were not the three who had used thrombolysis in hospital during training.

When I asked the doctors "What prevents you from using thrombolysis?" four said that extra work was involved. Reasons given for this were establishing a diagnosis of sufficient certainty and performing electrocardiography. Two of the three doctors who had used anistreplase did not report extra work. No doctor reported that financial considerations were a barrier. Four doctors thought that availability of the drug was a problem. The need for refrigeration and the long delays in replacing stock were commented on. When asked "How confident are you at using anistreplase?" half of the doctors said that they were confident to use it with support from ambulance staff or a nurse. Most wanted a trained person with them; three doctors wanted medical support before using anistreplase.

Solutions to the low uptake of prehospital thrombolysis lie in increasing doctors' confidence and giving reassurance about the safety of prehospital thrombolysis. Since 1992 the development of larger rotas for emergency medical care has changed the way that many doctors work. Cars with sophisticated equipment are becoming more common. To overcome problems with refrigeration and availability, perhaps streptokinase should be reconsidered as a prehospital thrombolytic agent.

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1 Vale L, Silcock J, Rawles J. An economic evaluation of thrombolysis in a remote rural community. *BMJ* 1997;314:570-2. (22 February.)

Rate of hysterectomy is lower among female doctors and lawyers' wives

EDITOR—In his editorial on the bill resulting from hysterectomy R J Lilford cites a study by Bunker and Brown, carried out 27 years ago.[1] The results of this study support his statement that the prevalence of hysterectomy among doctors' wives showed no difference from that among controls matched for social class.[2] The results were seriously flawed by the role of American economic barriers to medical care for the whole population due to lack of a universal health insurance.

We conducted a similar study in a homogeneous fee for service healthcare market (Switzerland) in which financial barriers to medical care for the whole population were largely removed 80 years ago.[3] Unlike Bunker and Brown, we used strictly the same methodology to collect and analyse data for each social class. Our results, contrary to Bunker and Brown's findings, show that the standardised rate of hysterectomy among women in the general population (n = 808; prevalence 15.70%) was significantly higher than that among female doctors (n = 433; 9.96%) and lawyers' wives (n = 188; 8.45%) ($P < 0.01$) and the same as that among other professionals with a university degree (n = 159; 13.88%).

Thus our results suggest that, in a fee for service market, as economic barriers to health care are removed so a social class gradient in consumption will appear. We also found that lawyers seem to be regarded by their doctors as special patients, probably because lawyer-patients are potentially more able to cause legal trouble if an adverse event or outcome related to the surgical procedure should happen.

A more recent study that we carried out on the lifetime prevalence of some surgical procedures in Switzerland shows that, for hysterectomy and other procedures, the most coveted surgical patients are the less well educated and best insured (in Switzerland, patients with private hospital insurance).[4] The prevalence of hysterectomy among generally insured patients was 12.2% (n = 2221) and that among privately insured patients was 18.1% (n = 1052) ($P < 0.001$). In this last group the lifetime prevalence of hysterectomy among less educated patients was 29.9% (n = 396) and that among highly educated patients was 12.9% (n = 468) ($P < 0.001$).

These results seem to suggest that the assumption that gynaecologists "exploit women for personal gain or take some sort of covert delight in the procedure"[1] is no longer to be rejected. Another of our studies showed that female gynaecologists performed about half as many hysterectomies (median yearly number 18) as male gynaecologists (median yearly number 34).[5] Perhaps fortunately for male patients, in that time no female urologists practised on the Swiss health market scene.

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1 Lilford RJ. Hysterectomy: will it pay the bills in 2007? *BMJ* 1997;314:160-1. (18 January.)
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Health workers need information from countries with better health indicators than Britain and the US

EDITOR—Meeting the information needs of public health workers in developing countries is an urgent problem.[1] Information has to be provided, but how best can this be done? The first public health institutions were established in England in the 19th century after the health effects of the Industrial Revolution were experienced. The advances in public health there had a strong influence in Europe and the United States. The approaches towards public health in the 20th century have been dominated by Britain and the United States. During the past 20 years, however, health in these two countries has lagged behind that in many other countries. For example, Japan's life expectancy and infant mortality have been the best for many years, whereas infant mortality in Britain and the United States did not even rank in the top 10.[2]

We argue that information flowing into developing countries should come not only from Britain and the United States but also from countries with successful public health programmes. In Medline during the past decade, however, more than half of the information on public health was from Britain and the United States, yet only 1.7% was from Japan and 0.01% from Iceland, the countries with the highest life expectancy. It might be better to model at least part of the public health programmes in Africa on the successes of Japan. These success stories can potentially be best told through the internet. We have described several possible ways of dealing with the language barrier to globalise health data.[3]

There are other key issues. Firstly, people working in public health should become familiar with information exchange through the internet. For this purpose we have conducted several training courses world wide such as the World Health Organisation/global health network joint programme internet training course in Japan (http://www.pitt.edu/~akira/course/home.htm). Secondly, world wide web mirror sites should be set up so that people can have faster access to the information. The global health disaster network was set up in this manner (http://hypnos.m.ehime-u.acjp/GHDNet/ in Japan, and http://www.pitt.edu/~ghdnet/GHDNet/ in the United States). Thirdly, we have to discuss how we can develop an infrastructure for the information with low band width connectivity, because only information with low band width reaches most of the developing countries that have access to the Internet.

There is little question that we have learnt much through the enormous amount of public health information from Britain and the United States. We can also, however, learn much from the areas with the best health indicators, which disproportionately provide less information than these two countries.

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Sentiweb remains efficient tool for nationwide surveillance of disease

EDITOR—Our paper on Sentiweb, the French electronic sentinel system for surveillance of communicable diseases on the world wide web, was accompanied by three commentaries.[1] In one of them Norman Noah was surprised by the low rate of reports, considering that (only?) 330 000 cases were notified in 12 years, leading to one case per doctor per week. Noah's calculations were not, however, appropriate. Some diseases shown on the internet (for example, chickenpox and diarrhoea) have been under surveillance for only six years. Estimates of nationwide incidences take into account the variable participation in the network and the network's representativeness. Eventually, other sources of information cross validate the system, such as the estimated number of cases of chickenpox each year (600 000); this number is of the same order of magnitude as a birth cohort in France, since around 90% of cases are known to be diagnosed by general practitioners and 95% of the population has been infected.

The system was conceived as a complement to the notifying system.[2] This was the consequence of close collaboration between INSERM and the French Department of Health. Rare events (for example, rabies) are obviously unlikely to be accurately detected through a sentinel system. However, measles was not notifiable after 1986, when the notification system collected less than 300 cases in a single year; the sentinel system estimated the actual incidence to be around 300 000 cases. Nowadays, with an estimate of more than 50 000 cases a year detected by general practitioners in France, the sentinel system remains an efficient tool for nationwide surveillance of the disease, although not for the detection of local outbreaks.

Do clinical cases of acute diarrhoea or influenza-like illness detected in primary care correspond to true cases? Preliminary results of a case-control study that we conducted, in addition to the surveillance, indicate that cases of acute diarrhoea in winter are not due to consumption of shellfish or tap water.[3] Moreover, general practitioners' attitudes to diagnosis, prescribing, and sick leave in the care of influenza-like illness were found to be similar whether the virus was influenza or respiratory syncytial virus (F Carrat *et al*, third international congress on options for the control of influenza, Cairns, Australia, 4-9 May 1996).

The last point debated by Noah concerned the huge number of maps and graphs available to net users. He sounds to us like a disappointed customer facing the catalogue of an airline company: "Several thousand destinations are provided; therefore I don't know where to go, and I would prefer a catalogue of domestic flights for my next holiday."

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Achievements in new deal for junior doctors' hours should be independently audited

EDITOR—Medicopolitical Digest comments on the new deal for junior doctors' hours, with its target date of 31 December 1996.[1] While the NHS Executive admits that there is still a hard core of problems to resolve, I believe that in many cases the methods of gathering data lead to poor quality data and unsatisfactory answers. It is all too common for an ambitious junior doctor, anxious about the allocation of a training number, to be drawn into collusion with his or her employing authority about hours of work. The commonest evidence for this has been the rush of accountants intent on reducing the amount of pay, whether or not the clinical team has achieved a reduction in hours of work. The result of these forces is that neither the trainee nor the institution has any interest in admitting the true working hours.

The most important advance would be realistic independent audit, which should not require young doctors to risk their career ambitions by seeming to be out of step with their seniors. Until this issue is resolved, many of the data gathered may be spurious.

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1 Beecham L. Taking forward the new deal on junior doctors' hours. *BMJ* 1997;314:448. (8 February.)