factors, we suggest that this has two profound implications: firstly, risk factors in the disease will be defined as those that alter expression of the precursor protein gene, and, secondly, effective treatments of Alzheimer's disease will be those targeted at modulating expression of the precursor protein gene.

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Chemotherapy in advanced ovarian cancer

SIR,—The Advanced Ovarian Cancer Trialists Group performed an overview of randomised trials of chemotherapy in advanced ovarian cancer.¹ I have questions about their conclusion favouring platinum chemotherapy.

They categorised 45 trials into five groups, and many of the trials seem to have had arms that could be included in more than one group. However, there are only four trials in two different groups, and only one trial in three groups. If a trial had an arm that could fit into two groups it should be used twice, and this should be done consistently, to increase the power of the study's findings. The median survivals approximated from the graphs (figs 1, 3, 5, 7, and 9) are 14 months for both arms in group I, 16 and 18 months in group II, 16 and 18 months in group III, 19 and 21 months in group IV, and 22 and 24 months in group V. Some of the difference in the median survival of apparently similar arms may be due to the exclusion of valid subgroups. This increased median survival from group I to group V may simply be due to stage creep, the Will Rogers phenomenon.²

The authors found no significant difference between combinations with and without platinum (comparison III) and also state that there is no evidence that non-platinum drug combinations are superior to non-platinum single agents (comparison I). A reasonable conclusion from these two statements is that there is no clear evidence that platinum based treatment is more effective than a single or non-platinum agent. The reason for stating that "immediate platinum based treatment was better than non-platinum based treatment" is not obvious as the confidence intervals of the relevant curves (figs 1, 3, and 5) show that treatment without a platinum based agent gave equal results.

Logically then, patients could be treated with a regimen such as oral chlorambucil, with com-

bination treatment being reserved for subsequent relapse as no difference in survival has been shown. Oral chlorambucil is well tolerated and can be taken as an outpatient and is cheaper than intravenous platinum based regimens. With platinum added into the cost of treatment as second line treatment there would still be advantages in terms of both cost and quality of life. This must be included as an arm in future trials.

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SIR,—We agree with many of D J Cruickshank's comments¹ on our overview of randomised clinical trials of chemotherapy in advanced ovarian cancer.² He emphasises that in the past clinical practice has been unduly influenced by small, inconclusive trials.

It is true that in the absence of any randomised trials incorporating an untreated control group there is no direct evidence that chemotherapy is beneficial in advanced ovarian cancer. Given the widespread routine use of chemotherapy, however, it would not currently be possible to conduct such a trial. Nevertheless, we are carrying out a trial in early stage disease in which patients are randomised to receive immediate or deferred adjuvant platinum based chemotherapy. This will run concurrently with another trial comparing carboplatin alone with cyclophosphamide, doxorubicin, and cisplatin in advanced disease. Although we agree that quality of life studies are extremely important, these can be placed in context only by accurate estimates of survival. Both of these two trials are "large simple trials," and within their flexible framework interested groups can incorporate assessment of quality of life. Indeed, one such study is already planned.

The trial comparing carboplatin with cyclophosphamide, doxorubicin, and cisplatin shows that we are interested in quality as well as quantity of survival. Although we do not agree that the regimen of cyclophosphamide, doxorubicin, and cisplatin is highly toxic, as some of the severe side effects can be controlled with modern antiemetic agents, it is less pleasant treatment than carboplatin alone. As existing information suggests that platinum based combinations² and, in particular, cyclophosphamide, doxorubicin, and cisplatin³ may improve survival, however, it is necessary to establish whether this is indeed so and the magnitude of any possible effect of treatment. Only then can we consider a reliable cost-benefit analysis of the treatments, including survival, toxicity, and quality of life. Studies of patients' attitudes have shown that they are willing to accept more aggressive treatments in return for very moderate survival benefits.⁴

As there is little reliable information on major prognostic factors in advanced disease the suggested "prognosis oriented treatment strategy" is not feasible at this time. We do, however, believe that further study is required and plan to investigate many prognostic factors when we update the overview next year.

Finally, power calculations were omitted from the article for reasons of space; they are stated clearly in the trial protocols. For the trial comparing carboplatin alone with cyclophosphamide, doxorubicin, and cisplatin in advanced disease, assuming a five year survival of 20%, 2000 patients would enable us to detect a 6% absolute or 30% relative improvement at five years (5% significance

level, 90% power). For the trial comparing immediate and deferred adjuvant platinum based chemotherapy in early disease, assuming a five year survival of 60%, 2000 patients would enable us to detect an absolute difference of 7% with the same significance level and power.

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Intravenous magnesium in suspected acute myocardial infarction

SIR,—In their overview of trials of intravenous magnesium salts in acute myocardial infarction Koon K Teo and colleagues point out¹ that the largest published study (the first Leicester trial) reported only those deaths occurring during the 24 hours for which magnesium sulphate or saline was infused.² We have now completed a long term follow up of the patients randomised in that study, which took place between October 1983 and May 1984. By using hospital and general practice records and the NHS Central Register we have obtained survival data on 96% of the patients at one year and 92% at five years. We have analysed the groups as randomised; the initial report was confined to those in whom myocardial infarction was subsequently confirmed.

The mortality odds ratio and its 95% confidence interval (magnesium:placebo) were 0.64 (0.31 to 1.33) at 28 days after randomisation, 0.77 (0.42 to 1.41) at one year, and 0.77 (0.47 to 1.26) at five years. If the 28 day data are used to recalculate the typical odds ratio for all seven studies included in the overview the point estimate is 0.52 (0.33 to 0.80), marginally nearer the null value but still suggesting that intravenous magnesium has a substantial protective effect.

Recruitment of about 2400 patients to the second Leicester study is due to be completed in February. The fourth international study of infarct survival, which examines an essentially identical magnesium regimen in a factorial design, has already enrolled over 5000 patients. A clear answer on this intriguing issue is therefore likely to be available before long.

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Urinary incontinence

SIR,—Though it is laudable to try to provide and evaluate conservative management of incontinence economically in the community, we think that

James O'Brien and colleagues' approach was too simplistic.¹

The premise that primary treatment of the symptoms of stress, urge, and mixed incontinence is simple is unfounded. In controlled trials the objective cure rate after pelvic floor exercise in women with genuine stress incontinence is low²; similarly, in women with detrusor instability bladder retraining is associated with a high long term relapse rate.³

In O'Brien and colleagues' study patients were treated on the basis of symptoms alone and no attempt was made to diagnose the cause of incontinence. As the correlation between urinary symptoms and urodynamic diagnosis is poor⁴ many patients will have been incorrectly treated, resulting in an apparent reduction in the efficacy of treatment. It is not surprising that patients with mixed symptoms had the poorest outcome, with only half reporting symptomatic improvement.

Patients who remain incontinent will become disillusioned and may seek no further medical advice, thinking that nothing can be done to help them. It is already difficult to convince patients that most of them can be cured, or their incontinence can at least be improved, by appropriate investigation and management.

The nature and duration of follow up were inadequate; no objective measures of severity of leakage were used, and no assessment of the results of treatment was continued beyond 12 weeks.

We believe that, with few exceptions (notably elderly people), incontinent patients require some basic investigation, often including urodynamic assessment, before treatment. Outcome should be carefully monitored and assessed objectively whenever possible.

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Potassium concentrations in irradiated blood

SIR,—G Dinning and colleagues report increased concentrations of potassium in irradiated blood.¹ The Royal Liverpool University Hospital receives 65% of its blood as SAG-M blood; this blood has virtually all its plasma removed and replaced with an isotonic nutrient solution (saline, adenine, glucose, mannitol).

We measured potassium concentrations in SAG-M blood after irradiation (with 15 Gy). The concentrations were higher in SAG-M blood than whole blood throughout storage (table). After irradiation they increased in a fashion similar to concentrations in whole blood and plasma reduced blood,¹ values as high as those in non-irradiated

Potassium concentrations (mmol/l) in irradiated whole blood and SAG-M blood

	Days after collection			
	9	25	33	35
Whole blood	11	15.3	16	27
Irradiated whole blood	19.5	27.3	32.5	38.6
SAG-M blood	20	30	38	60.5
Irradiated SAG-M blood	30.7	52.5	62	72

blood at its expiry date (35 days' storage) being attained after 15 days' storage. We therefore recommend that any blood, but particularly SAG-M blood, irradiated at this hospital should be as fresh as possible and should be administered as soon after irradiation as practicable, and we do not store irradiated blood for more than 48 hours.

Dinning and colleagues suggest that unused irradiated blood may be cross matched for other patients. We do not recommend this policy for patients who would not normally receive irradiated blood. Luban and Ness outline theoretical risks of such a policy in view of changes to DNA structure and repair induced by irradiation and the possibility of producing sister chromatid exchanges, all of which may predispose to primary or secondary malignancy or chromosomal damage.²

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The health of the nation

SIR,—With regard to the many letters published recently concerning *The Health of the Nation*, may I add that the role of early intervention concerning emotional stress disorder in young children is not mentioned in recent documents on child surveillance that I have read, although the Royal College of General Practitioners states that emotional aspects should always be borne in mind.¹

Major (and minor) adult psychiatric illness is often costly to treat and entails considerable suffering. Studies show connections between childhood psychological problems and subsequent illness. Research shows the considerable value, clinically and financially, of surveillance for emotional disorder in early childhood. The annual research review of the International Association of Child Psychology and Psychiatry (of which I am southwest chair) describes some of these studies.² For example, an esteemed unit in New York described early intervention in infantile autism as successful. (Lack of eye contact between mother and infant was one diagnostic item.) Studies from Scotland indicate that the value of postnatal counselling by a health visitor diminishes the need for antidepressants.³

Recent work by Nicol in Leicester (and Kolvin in Newcastle) indicates the value of different degrees of parent, group, and family therapy.^{2,4} They screened a population and offered treatment for children and mothers with emotional problems rather than treating patients presenting themselves.

Richman's work at the Hospital for Sick Children, Great Ormond Street, shows that a large percentage of children with symptoms at the age of 3 continue to have them at the age of 8.⁵ All children thus "do not grow out of" enuresis, sleep disorders, etc.

I have used a mother-baby interaction scale (valid from birth to 2 years) which could be incorporated in a surveillance document. Often parents are not aware of emotional problems in themselves and their children. At surveillance, problems can be picked up about which parents may not have approached their medical practitioners.^{6,8}

Incidentally, follow up studies show the upset caused by mother-baby separation and long term effects on the physiological and immune systems.⁹

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Endometrial resection or abdominal hysterectomy in menorrhagia?

SIR,—In the past obstetric and gynaecological innovations have been enthusiastically embraced and have become accepted practice without proper evaluation. Disentangling the advantages and disadvantages, as with cervical cerclage, can be extremely laborious. Michael J Gannon and colleagues have made a creditable comparison between endometrial resection and abdominal hysterectomy for dysfunctional uterine bleeding.¹ More than 4000 women have now been treated by endometrial resection, and the authors' honest reporting of the problems that they have experienced with the new method is welcome; several serious, including some fatal, complications have occurred at other centres.

The costings given in the paper do not include costs for either pelvic ultrasonography or repeat endometrial ablation. In terms of relieving symptoms the failure rate of 16% for endometrial resection is high compared with that for hysterectomy.

The authors do not explain why contraceptive advice was based on the presence or absence of cyclical bleeding. Does this correlate with tubal patency? The pregnancy that occurred must be regarded as profoundly disturbing. Endometrial resection is, after all, intended to induce amenorrhoea, and an early pregnancy might therefore be unsuspected. The gestational age at which this pregnancy was detected is not stated. Though the psychological morbidity associated with early termination of unwanted pregnancy is low, a woman who has a second trimester termination after endometrial ablation might well suffer from conflicting feelings. With increasing gestation any consequences of placenta accreta presumably worsen. The postoperative progress after endometrial resection has been carefully assessed, but practice and advice after hysterectomy seem to be based on tradition.

The suggestion that vaginal hysterectomy might be a better comparison for endometrial resection prompted a review of 23 recent vaginal hysterectomies at Prince Philip Hospital, Llanelli, and West Wales General Hospital, Carmarthen. In addition to dysfunctional bleeding pathological findings included adenomyosis, fibroids, cervical intraepithelial neoplasia, and atypical hyperplasia. The operating time was 20-57 (median 30) minutes and the hospital stay 4-9 (median 5) days. At postoperative review four women had pelvic pain or vault tenderness and seven had vault granulation.

This prompted a review of routine practice. A 20 minute technique for vaginal hysterectomy has been described,² as has early discharge after this operation.³ Data corresponding to the criteria used to assess endometrial resection (the duration of bleeding or serosanguinous discharge and subjective assessment of recovery time) will be