Letters

Rationing in response to NHS deficits: rural patients are likely to be affected most See News, p 1426

EDITOR-News that pressing financial problems have caused NHS trusts in Suffolk to set new "thresholds" to treatments such as joint replacements reinforces concerns raised by a recent BMA survey of medical directors of trusts in which over a third of respondents anticipated reductions of key services in response to funding shortfalls.1 What has hitherto escaped comment is how cuts in services are far more likely to be felt in some parts of the country than others.

Deficits in the NHS are invariably presented as a problem of financial mismanagement, but the pattern of deficits shows that the current resource allocation model discriminates against particular communities. According to the recently published accounts for 2004-5,3 89 out of 303 (30%) English primary care trusts ended the year in deficit. The table shows how 301 of these trusts are distributed accorded to fifths of deprivation and rurality.

Primary care trusts serving populations that are in both the most rural and the least deprived fifth were most likely to be in financial difficulties. Seventeen of the 25 (68%) in this category were in deficit. These trusts received the lowest funding allocation per head (£995). By contrast, only 3% (one of 34) of the primary care trusts serving populations that are in both the most urban and the most deprived fifths failed to break even in 2004-5. These trusts received the highest funding allocations per head (£1405)

This shows that poor financial management can at best only partly explain why some trusts are in deficit. The pattern of deficits implies that NHS funding provides insufficient resources for rural areas, for comparatively affluent areas, and, most particularly, for areas that are both rural and affluent. The risk is that such measures will

result in NHS services being subject to a new postcode lottery, in which rural residents are more likely to lose out.

Sheena Asthana professor of health policy School of Sociology, Politics and Law, University of Plymouth, Plymouth PL4 8AA sasthana@plymouth.ac.uk

Alex Gibson innovation and research fellow Faculty of Health and Social Work, University of Plymouth

Competing interests: None declared.

- 1 Coombes R. Rationing of joint replacements raises fears of further cuts, *BMJ* 2005;331:1290. (3 December.)
- 2 British Medical Association. Funding difficulties in the NHS. A survey of medical directors of trusts in England. London: BMA, 2005. www.bma.org.uk/ap.nsf/content/ nhsfundingdifficulty?OpenDocument&Highlight = 2,NHS, trust,shortfall (accessed 7 Dec 2005).
- 3 Department of Health. NHS organisations annual accounts surplus and deficits 2004-05. London: DoH, 2005. www.dh.gov.uk/PublicationsAndStatistics/Publications/ PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID = 4119175&chk = JuzTDZ (accessed 7 Dec 2005).

Rationing joint replacements

Trust's decision seems to be based on prejudice or attributing blame...

EDITOR-The decision of the East Suffolk primary care trusts not to fund joint replacements for patients unless the patient has a body mass index (BMI) below 30 and conservative means have failed to alleviate the pain and disability breaches basic principles of health care that do not seek to judge patients for their illness.1 The decision confuses three separate questions: does obesity cause osteoarthritis, does weight loss improve it, and is surgery more dangerous or less successful in obese patients?

Obesity and risk for osteoarthritis of the knee (especially bilateral) are associated, as is a response of symptoms to weight loss2; the links with hip osteoarthritis are less clear.

Weight loss is a logical initial management for painful knee osteoarthritis but does not obviate the potential benefit of surgery for symptomatic patients, whether they have lost weight or have been able to reduce their BMI below 30.

No evidence supports withholding joint replacement from obese people, even on utilitarian grounds. For knee replacement, there is "no evidence that age, gender, or obesity is a strong predictor of functional outcomes."3 A UK health technology assessment of hip replacement concluded that obese patients (with a BMI > 30) could benefit from total primary hip arthroplasties without cement and that obesity did not noticeably increase the operative risk.4 Chan et al found no significant difference in the improvement in scores (of quality of life) between the non-obese and obese groups, concluding that relative body weight alone does not influence the benefit derived from primary total hip arthroplasty.5

Since obesity does not increase the risks diminish the benefits of joint replacement, the trust's decision to deny such treatment seems to be based on prejudice or attribution of fault, or both. Logically extended, such a policy would deny treatment to, among others, smokers, most patients with HIV infection, and those who sustain sports injury.

Nicholas Finer consultant in obesity medicine Addenbrooke's Hospital, Cambridge CB2 2QQ nf237@medschl.cam.ac.uk

Competing interests: None declared.

- Coombes R. Rationing of joint replacements raises fears of further cuts. *BMJ* 2005;331:1290.(3 December.)
 Nevitt MC. Obesity outcomes in disease management: clinical outcomes for osteoarthritis. *Obes Res* 2002; 10(suppl 1):33S-37S.
- 10(suppl 1):353-378.
 3 Department of Health and Human Services. Total knee replacement. Rockville, MD: Agency for Healthcare Research and Quality, Department of Health and Human Services, 2003. (Evidence report/technology assessment No 86.)
 4 Faulkner A, Kennedy LG, Baxter K, Donovan J, Wilkinson
- M, Bevan G. Effectiveness of hip prostheses in primary total hip replacement: a critical review of evidence and an economic model. Health Technol Assess 1998;2:1-133.
- 5 Chan CL, Villar RN. Obesity and quality of life after primary hip arthroplasty. J Bone Joint Surg Br 1996;78:855-6.

Distribution of primary care trusts in deficit, 2004-5. Values are proportions (percentages) unless stated otherwise

| | Rurality | | | | | | | | | | | | - Average primary care trust per |
|---|------------------|--------|-------|------|-------|------|-------|--------|-------------------|------|--------|------|----------------------------------|
| Deprivation | Most urban fifth | | 2nd | | 3rd | | 4th | | Least urban fifth | | Total | | head turnover, 2004-5 (£) |
| Most deprived fifth | 1/34 | (3) | 3/19 | (19) | 0/7 | (0) | | N/a | N/a | | 4/60 | (7) | 1359 |
| 2nd | 2/15 | (13) | 2/22 | (9) | 0/10 | (0) | 1/8 | (12.5) | 1/5 | (20) | 6/60 | (10) | 1209 |
| 3rd | 2/8 | (25) | 1/6 | (17) | 5/16 | (31) | 6/19 | (32) | 7/11 | (64) | 21/60 | (35) | 1133 |
| 4th | 2/3 | (67) | 2/9 | (22) | 7/13 | (53) | 7/16 | (44) | 3/19 | (16) | 21/60 | (35) | 1093 |
| Least deprived fifth | 0/1 | (0) | 3/4 | (75) | 8/14 | (57) | 9/17 | (53) | 17/25 | (68) | 37/61 | (61) | 1013 |
| Total | 7/61 | (11.5) | 11/60 | (18) | 20/60 | (33) | 23/60 | (38) | 28/60 | (47) | 89/301 | (30) | |
| Average primary care trust per head turnover, 2004-5 (£) | 1321 | | 1218 | | 1110 | | 1081 | | 1072 | | | | |

N/a=not applicable.

... and is false economy resulting in overall damage

Editor-Rationing hip replacements may save costs for commissioners, but it cannot in this timescale save any costs to providers in the NHS—which means, money is wasted.1

Delaying operations on "punitive" grounds may increase long term costs. Personal experience shows that delaying joint replacement surgery causes deterioration of functional capacity, which is difficult or impossible to reverse after later operation. What is the evidence that these strict conditions are not in the longer term damaging?

This is rationing by any other name—or choice if your commissioner is not overspent, if your body mass index is not too high, and you do not have a major disability. A curious definition.

Martin W McNicol retired Cirencester, Gloucestershire GL7 1FA mcnicol@globalnet.co.uk

Competing interests: None declared.

1 Coombes R. Rationing of joint replacements raises fears of further cuts. BMJ 2005;331:1290. (3 December.)

District general hospitals have a future in truly rural areas

EDITOR-Ham clearly has the governments of both England and Wales in tow with his ideas on market reform in the NHS.1 To rationalise services that may be duplicated in several hospitals within a radius of 10-15 miles, as may be found in many cities or other densely populated areas, is certainly sensible. However, none of Ham's ideas answers the question, "How do you maintain the skill mix to deal with acute life threatening conditions in a hospital that is 30 miles from the next district general hospital up the road?'

The answer, of course, is that you have to maintain it as a district general hospital in its own right. To do that you cannot chip away at some services and hope that the others will be maintained. For example, if you acknowledge that you need somebody around with the skills to deal with a ruptured spleen or a massive haematemesis, then you have to accept that you won't get such a person if you expect him or her the rest of the time to deal only with lumps and bumps. We know this well in Pembrokeshire.

Peter J Milewski consultant in general surgery Withybush Hospital, Haverfordwest, Pembrokeshire peter.milewski@gmail.com

Competing interests: PJM is a consultant in a truly rural hospital.

 $1\,$ Ham C. Does the district general hospital have a future? $BMJ\,2005;\!331:\!1331-\!3.(3$ December.)

Commissioning perhaps shouldn't follow the American way

Editor-Donaldson and Ruta make a compelling case for the adaptation, rather than replication, of US health systems in England.1 That general practices should increase

in size to manage populations of 25 000-30 000 makes organisational and economic sense, and those practices that achieve this will, no doubt, be the survivors in the world of contestability ushered in by the forthcoming white paper on care outside hospitals.

However, this suggestion deals only with the provider side of primary care. For the purposes of commissioning, whether based at the level of the practice or primary care trust, populations of 30 000 are almost certainly too small. This size of patient base exhibits too many variations in referral rates and secondary care activity to accommodate commissioning budgets safely, and these "super practices," if contracting in secondary care professionals, risk fragmentation and unsustainability of the secondary care

The government's move towards greater health and social services integration is best served by coterminosity of health and local authority boundaries. Local authority populations of 100 000 or more and their constituent general practices are the ideal model for clinically led joint commissioning (health and social care) of a vertically integrated model.

The authors are dismissive of the national tariff, and, to an extent, rightly so. At present tariffs are too crude and simplistic to be helpful in a quasi market economy. Their application is too rigid to allow for service pathway alterations. They may, however, serve as a benchmark-a "recommended retail price"-which NHS commissioners would see as a maximum price to pay for a "unit" of activity, but with local flexibility to manage the market more sensitively as activity is increasingly devolved into the community.

John Hughes clinical director outh East Hants Primary Care Trust Cluster, Waterlooville, Hampshire PO7 7GP jrhughes@nildram.co.uk

Competing interests: None declared.

1 Donaldson C, Ruta D. Should the NHS follow the American way? BMJ 2005;331:1328-30. (3 December.)

US experience of smoke-free prisons

EDITOR-O'Dowd reports that a smoking ban in prisons would lead to more assaults on staff.1 Increasing numbers of correctional facilities in the United States have become smoke-free and made tobacco, matches, and lighters contraband. Most experience so far has not shown the feared difficulties arising when facilities become completely tobaccofree. Most programmes note that the issues around staff tobacco use at the facility are more challenging than those around prisoners' use.

A recent report indicated that 77% of US facilities surveyed in 2003 disallow tobacco use for prisoners, although 79% of them allow staff to use tobacco on the premises2; various programmes have noted some difficulty resulting from this. The transition process is not minimal, and some pro-

grammes have reported difficulties, including amplification of discontent among prisoners and staff. During the transition period some programmes have made nicotine replacement therapy available, although this was used by a small fraction of the populations. To our knowledge, no facilities that have instituted smoking bans have reversed that decision. In other mental health and addictions settings a critical review of 22 published studies found no major effects in behavioural indicators of unrest or compliance.3

On admission to a smoke-free jail our patients have repeatedly reported very little difficulty with stopping tobacco use, and that during the initial days and weeks, thoughts and energy are directed to far more pressing concerns. Stopping is different from quitting, and about 97% have returned to tobacco use by six months after release (R W Tuthill et al, 26th national conference on correctional health care, Nashville, Tennessee, October 2002).

Effective tobacco cessation and relapse prevention programmes are needed for people passing through the correctional system. A tobacco educational curriculum has been created and has been well accepted by prisoners and staff, though tobacco use outcomes have not yet been assessed.4

Thomas Lincoln *physician* Baystate Medical Center, Springfield, MA 01199, UŚA

thomas.lincoln@bhs.org

R Scott Chavez vice president National Commission on Correctional Health Care, 1145 W Diversey Parkway, Chicago, IL 60614,

Elizabeth Langmore-Avila substance abuse clinician 160 East Hadley Road, Amherst, MA 01002, USA

Competing interests: None declared.

- O'Dowd A. Smoking ban in prisons would lead to more assaults on staff. BMJ 2005;331:1228. (26 November.)
 Chavez RS, Oto-Kent DS, Porter J, Brown K, Quirk L, Lewis S. Tobacco policy, cessation, and education in correctional facilities. Chicago, It.: National Commission on Correc-tional Health Care and National Network on Tobacco Prevention and Poverty, 2005.
- 3 El-Guebaly N, Cathcart J, Currie S, Brown D, Gloster S. Public health and therapeutic aspects of smoking bans in mental health and addiction settings. *Psychiatr Serv* 2002;
- 4 National Commission on Correctional Health Care and National Network on Tobacco Prevention and Poverty. Tobacco cessation for correctional populations: a health education manual. 2005. www.ncchc.org/pubs/catalog.html#tobacco_cessation (accessed 8 Dec 2005).

Risk of gastrointestinal effects with COX-2 inhibitors and **NSAIDs**

Study conclusions do not reflect findings for celecoxib

Editor—The conclusions drawn by Hippisley-Cox et al do not accurately reflect the data as presented.1

This study found important differences between celecoxib and the studied nonsteroidal anti-inflammatory drugs (NSAIDs) in terms of the risk of adverse gastrointestinal effects. Specifically, celecoxib was the only treatment that did not significantly increase the risk of such adverse events

(adjusted relative risk 1.11, 95% confidence interval 0.87 to 1.41) compared with control patients. The authors comment that the number of patients taking celecoxib was low, yet the upper limit of the 95% CI for celecoxib is less than the lower limits for naproxen (1.73), diclofenac (1.78), other NSAIDs (1.43), and aspirin (1.49)supporting the relative gastrointestinal safety of celecoxib.

The findings are consistent with the results of other studies. NSAIDs typically increase by twofold to fourfold the risks of a gastrointestinal bleed. For example, Mamdani et al studied 1.3 million elderly patients in the Canadian population and found that celecoxib was not associated with increased risk of admission for gastrointestinal haemorrhage, as opposed to the significantly increased risk seen with other NSAIDs.2

The conclusions of the article, as well as its press release, do not fully acknowledge safety differences that the data showed among various arthritis treatment options. In this study, celecoxib had the lowest risk of gastrointestinal complications-important information for doctors and patients who are making health decisions.

Joe Feczko chief medical officer Pfizer, New York, NY 10017, USA $rscmoppgp\hbox{-} JoeFeczko@pfizer.com$

Competing interests: JF is an employee of Pfizer.

- 1 Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal antiinflammatory drugs: population based nested case-control analysis. *BMJ* 2005;331:1310-6. (3 December.)
- 2 Mamdani M, Rochon PA, Juurlink DN, Kopp A, Anderson GM, Naglie G, et al. Observational study of upper gastrointestinal haemorrhage in elderly patients given selective cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs. *BMJ* 2002;325:624-7.

How strong is the evidence?

Editor—The major conclusion drawn from the nested case-control study by Hippisley-Cox et al was that no consistent evidence was found of enhanced safety against gastrointestinal events with any of the new cyclo-oxygenase-2 (COX-2) inhibitors compared with non-selective non-steroidal antiinflammatory drugs (NSAIDs).

The adjusted odds ratio for current use of rofecoxib in patients currently taking aspirin was 2.98 (2.24 to 3.99) whereas it was 1.22 (0.97 to 1.54) in those not currently taking aspirin. While denoting a strong interaction between rofecoxib and aspirin, these data do not support the view of a significant increased hazard of gastrointestinal outcome in patients taking rofecoxib alone.

The authors acknowledged that any observational study may be subject to residual confounding that cannot be fully corrected for. In this respect, the present study was based on drug prescriptions and not actual drug consumption. A low compliance rate with a given drug might result in an improved gastrointestinal safety profile, and vice versa. Unfortunately, whether the

adherence to drug treatment was similar across all NSAIDs studied has not been

Bernard G Bannwarth professor of therapeutics University Hospital, 33076 Bordeaux, France bernard.bannwarth@u-bordeaux2.fr

Competing interests: BGB has been an invited speaker at Merck sponsored symposia and has participated in clinical studies sponsored by

1 Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. *BMJ* 2005;331:1310-6. (3 December.)

Why were patients at major risk excluded?

EDITOR-One of the strongest risk factors for gastrointestinal toxicity induced by non-steroidal anti-inflammatory

(NSAIDs) is known to be previous events. Hippisley-Cox et al excluded patients who had already had a diagnosis of an adverse upper gastrointestinal event before the study period.1 This removes patients at high risk from the analysis and introduces a fundamental bias. The large majority of the prescriptions of selective COX-2 inhibitors might well have been

given to high risk patients who were subsequently excluded from the analysis.

The authors also do not provide the crude number of patients with concurrent prescriptions of ulcer healing drugs by each NSAID. The vast majority of ulcer healing drugs may well have been prescribed to patients taking a non-selective NSAID.

Another issue is the effect of concurrent anti-inflammatory drugs. The odds ratios were adjusted for each other NSAID group, smoking, comorbidity, deprivation, and use of selective serotonin reuptake inhibitors, tricyclic antidepressants, statins, aspirin, and ulcer healing drugs. But it is important not only to adjust for previous NSAID use but also to consider how many different drugs had been used until index, their timing, and their nature. The gastrointestinal adverse effects of NSAIDs may persist for a long time, thus interacting with the next drug.

The conclusions do not reflect the results, at least in part. If patients taking celecoxib were too few what is the sense in comparing a class of non-selective NSAIDs with one drug (rofecoxib)?

Luca Puccetti president Promed Galileo Medical Association, Pisa 56011, lucpucce@promedgalileo.org

Competing interests: None declared.

1 Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking cyclooxygenase-2 inhibitors or conventional non-steroidal antiinflammatory drugs: population based nested case-control analysis. BMJ 2005;331:1310-6. (3 December.)

COX-2 inhibitors were thought of as a safe option

EDITOR-The study by Hippisley-Cox et al into the safety of cyclo-oxygenase-2 (COX-2) inhibitors and non-steroidal antiinflammatory drugs (NSAIDS) is subject to more indication bias than they suggest.1

When the study began, five years ago, COX-2 inhibitors were widely regarded as safer to prescribe in patients at high risk of developing gastrointestinal side effects than NSAIDs,2 although there were doubts over their cardiovascular safety.3 Working in general practice at the time, we saw COX-2 inhibitors used in primary care patients who had mild upper gastrointestinal symptoms or history, as a safe option. They were prescribed particularly in elderly people, in whom opiate analgesics often cause significant adverse effects. This practice would

have led to a higher risk cohort of patients being prescribed COX-2 inhibitors rather than NSAIDs, thus reducing the apparent safety of COX-2 inhibitors in this study.

Additionally, during the study period both ulcer healing drugs and NSAIDs were readily available over the counter. The study relied on using computerised pre-

scribing records from general practices as the main source of prescribing data. This neglects the confounding influence of over the counter drugs which have an important influence on the prevalence of gastrointestinal disease.4 5

Michael R Lewis general practitioner Welshpool Medical Centre, Powys SY21 7ER Michael.Lewis@gp-w96010.wales.nhs.uk

Diana Kay general practitioner Cheam Family Practice, Sutton, Surrey SM1 2HD

Competing interests: None declared.

- 1 Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. *BMJ* 2005;331:1310-6. (3 December.)
- 2 Deeks JD, Smith LA, Bradley MD. Efficacy, tolerability, and upper gastrointestinal safety of celecoxib for treatment of osteoarthritis and rheumatoid arthritis: systematic review of randomized controlled trials. *BMJ* 2002:325:619.

 3 Jones R. Efficacy and safety of COX-2 inhibitors. *BMJ*
- 2002;325:607-8.
- Bateman DN, Kennedy JG. Non-steroidal anti-inflammatory drugs and elderly patients. *BMJ* 1995;310: 4 Bateman DN,
- 5 Andersen M, Schou JS. Are H2 receptor antagonists safe over the counter drugs? *BMJ* 1994;309:493-4.

What does evidence from randomised trials show about celecoxib?

EDITOR-With reference to Feczko's comments (first letter in this cluster), Hippisley-Cox et al's study was an observational study.1 This occupies a lower place on the hierarchy of evidence than large, prospective randomised controlled trials measuring outcomes that are important to patients (patient oriented evidence that matters, or

The only POEM evidence for celecoxib is the CLASS study.2 CLASS showed no significant difference between celecoxib and

the comparators (diclofenac and ibuprofen) in terms of the primary outcome of the study-gastrointestinal ulcer complications.3 Only when a post-hoc sub-group analysis of these data was performed in those not taking aspirin was a significant benefit seen (with a P value of 0.04). This was one of over 34 post-hoc analyses performed on this study (so, by chance, we would expect at least one of these to show a difference with a P value slightly less than 0.05).4 Others have recently highlighted the folly of post-hoc subgroup analyses where the primary end point does not show a significant difference.5

The regulators in the USA and in Europe have concluded that the data from the CLASS study do not show a meaningful benefit for celecoxib (www.fda.gov/bbs/ topics/ANSWERS/2002/ANS01151.html). That the prescribing of this drug continues to increase despite the lack of good quality evidence for its usefulness in providing a benefit to patients is disappointing.

Perhaps we should stop arguing about the wording of the conclusions of hypothesis generating data (like those of Hippisley-Cox et al). Although such data are interesting, they do not inform our practice in the same way that a negative prospective randomised controlled trial does.

Jonathan L Underhill assistant director, education and development
National Prescribing Centre, The Infirmary, Liverpool L69 3GF jonathan.underhill@npc.nhs.uk

Competing interests: None declared.

- 1 Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal antiinflammatory drugs: population based nested case-control analysis. *BMJ* 2005;331:1310-6. (3 December.)

 2 Silverstein FE, Faich G, Goldstein GL. Simon LS, Pincus T,
- Whelton A, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized
- controlled trial. Celecoxib Long-term Arthritis Safety Study. JAMA 2000;284:1247-55.

 3 Jüni P, Rutjes AWS, Dieppe PA. Are selective COX 2 inhibitors superior to traditional non-steroidal anti-inflammatory drugs? BMJ 2002;324:1287-8.

 4 Lu HL. Statistical reviewer briefing document for the advisory committee. Available at: www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_04_stats.doc (accessed 8 Dec 2005.)

 5 Freementle N. Havenell, A. and A. and A. Statistical controlled the controlled to the
- 5 Freemantle N. How well does the evidence on pioglitazone back up researchers' claims for a reduction in macrovascular events? BMJ 2005;331:836-8. (8 October.)

Recessive disorders and consanguineous marriage

EDITOR-Dyer in his news item misquotes Alison Shaw. The doubling of risk from 2% to 4% with marriage of cousins is for all congenital or genetic disorders, not recessive disorders, which are much less common in the white population.

In Blackburn the Asian population has a 12-fold increased risk of recessive disorders compared with the white population, with 13 new recessive disorders per 1000 births (S Kowariwalla, J Benson, unpublished data, 2002). These figures are similar to reported data.2

The burden of illness and handicap from these recessive disorders is huge. Individual recessive disorders tend to cluster in family groups. The simple message for the Asian community that favours cousin marriage is that if a recessive disorder is found in the family genetic advice must be sought before marrying and having chil-

In most recessive disorders in our Asian population a DNA diagnosis is still not possible. This means that many families will need to consider non-consanguineous marriage as the only way to lower the risk. For family groups with no known recessive disorder, cousin marriage remains a reasonable option.

John W T Benson consultant paediatrician Queens Park Hospital, Blackburn BB2 3HH john.benson@elht.nhs.uk

Competing interests: None declared.

- 1 Dyer O. MP is criticised for saying that marriage of first cousins is a health problem. *BMJ* 2005;331: 1292. (3 December.)
- December.)

 2 Modell B, Darr A. Genetic counselling and customary consanguineous marriage. Nat Rev 2002, 3: 225-229.

 3 Bundey S, Alam H. A five-year prospective study of the health of children in different ethnic groups, with particular reference to the effect of inbreeding. Eur J Hum Genet 1993;1:206-19.

Giving steroids before elective caesarean section

Authors respond to editorial

EDITOR-We reported the outcome of a randomised trial of antenatal betamethasone before elective caesarean section at term, showing a reduction of more than 50% in admission with respiratory distress for babies delivered at 37-39 weeks (BMI) 24 September, p 662). Of the 35 babies admitted with respiratory distress, 19 control babies had transient tachypnoea and five had respiratory distress syndrome, compared with 10 babies with transient tachypnoea and one with respiratory distress syndrome in the intervention group. Fourteen control babies required intensive care, three with respiratory distress syndrome requiring ventilation for two to five days, with a 12-18 day stay, whereas only two in the intervention group received intensive

We postulated that the reduced incidence of transient tachypnoea with antenatal betamethasone may result from an effect on the expression of the epithelial channel gene allowing the lung to switch from fluid secretion to fluid absorption. Fiori's electronic response to our paper provides evidence for an additional factor, enhanced surfactant production. The presence of lung fluid is likely to delay surfactant production, leading to a further decrease in lung compliance seen in transient tachypnoea.

In the accompanying editorial Steer raises concerns about the long term consequences of giving antenatal steroids by reporting the outcome of follow-up studies where multiple two weekly courses of antenatal steroids were given from 24 weeks' gestation onwards and high dose intravenous postnatal courses of corticosteroid were prescribed for the very preterm to prevent chronic lung disease.1 He then raised the spectre of thalidomide and diethylstilbestrol in pregnancy, in which mass prescribing and the lack of long term follow-up research led to well reported serious consequences. These drugs were used early in pregnancy during early embryogenesis. Steer concludes that "giving steroids ... even as a single course, remains questionable."

Although we understand Steer's concern, the Cochrane review in 2003 and the evidence based guideline of the Royal College of Obstetricians and Gynaecologists on the use of antenatal corticosteroids to prevent respiratory distress syndrome conclude that a single course of antenatal corticosteroid has no adverse effect on physical growth, neurological or cognitive outcome, or infection in child or mother.2 3 The royal college's guideline synthesises five papers following more than 1500 survivors from randomised trials or cohort studies of antenatal corticosteroids for up to 20 years. We have reviewed all five papers, together with another published since the guideline and Dalziel et al's paper extending follow-up to 31 years.45 We find the college guideline rigorous and appropriate.

The risk of Steer's recommendation is discouraging others from discussing and offering a simple, safe, and effective evidence based preventive measure to women who, for whatever reason, require or plan an elective section before 39 weeks.

PR Stutchfield consultant paediatrician Conwy and Denbighshire NHS Trust, Glan Clwyd Hospital, Rhyl, Denbighshire LL18 5UJ DrPeter.Stutchfield@cd-tr.wales.nhs.uk

R Whitaker trial statistician Institute of Medical and Social Care Research, University of Wales Bangor LL57 2PX

Competing interests: None declared.

- Steer P J. Giving steroids before elective caesarean section.
 BMJ 2005;331:645-6. (24 September.)
 Crowley P, Roberts D, Dalziel S, Shaw BNJ. Antenatal corticosteroids to accelerate fetal lung maturation for women at risk of preterm birth. (Protocol) Cochrane Database Syst Rev 2003;4:CD004454.
- 3 Royal College of Obstetricians and Gynaecologists Scientific Advisory Committee, Antenatal corticosteroids to breven
- titic Advisory Committee. Antenatal corticosteroids to prevent respiratory distress syndrome. 2nd ed. London: RCOG Press, 2004:1-9. (RCOG guidelines No 7.)

 4 Dalziel SR, Liang A, Parag V, Rodgers A, Hardin JE. Blood pressure at six years of age after prenatal exposure to betamethasone: follow up results of a randomised controlled trial. Pediatrics 2004;114:e373-7.
- The strain reductive 2004;114:e57-57.

 Dalziel SR, Lim VK, Lambert A, McCarthy D, Parag V, Rodgers A, Harding JE. Antenatal exposure to betamethasone: psychological functioning and health related quality of life 31 years after inclusion in randomised controlled trial. BMJ 2005;331:665-8. (24 September.)

European subsidies and developing countries

EDITOR-There is intuitive appeal in suggesting that excess food production in Europe has resulted in farmers from developing countries not being able to compete in the international agricultural market.1 A more important question, however, is how has failure to compete influenced the life of country farmers or citizens in developing countries?

Most inhabitants of developing nations are rural dwellers-for example, over 70% of Nigeria's population.2 Most are subsistence farmers who produce foods for family and local markets. They have never traded internationally and may never do so. However, a few urban dwellers are professional farmers practising medium to large scale mechanised farming. These are the few who have been unable to compete. Their food productions never served the needs of the larger population. Therefore, while the suggested changes in the European agricultural policy might improve the outlook for obesity and healthy nutrition in developing countries, they are likely to widen inequalities in developing countries by favouring the already favoured mechanised farmers.

What is needed more urgently so far as developing countries are concerned is increased national political commitment to stimulating growth through sound national social and economic policy. If, for example, African leaders subsidised rural agriculture, growth in that sector, as well as eradication of poverty and hunger, would necessarily follow in spite of European agricultural policy.

Kelechi E Nnoaham specialist registrar in public health

North Oxfordshire Primary Care Trust, Adderbury, Oxfordshire OX17 3NS kcnnoaham@yahoo.com

Competing interests: None declared.

- 1 Elinder LS. Obesity, hunger, and agriculture: the damaging role of subsidies. *BMJ* 2005;331:1333-6. (3 December.)
- 2 US Library of Congress. Nigeria. Available at http:// countrystudies.us/nigeria/34.htm. (accessed 2 Nov 2005).

New TB vaccine granted orphan drug status

EDITOR—We report how orphan drug status is also relevant for global diseases most prevalent in developing countries.

One third of the world's population is chronically infected with tuberculosis (TB), and 500 children die every day.¹ The current BCG vaccine protects children against disseminated disease but confers variable protection against lung disease in adults. A recombinant modified vaccinia virus Ankara expressing the antigen 85A gene from *Mycobacterium tuberculosis* (MVA85A) is being developed to enhance the immunogenicity and protective efficacy of BCG.² This vaccine was recently designated an orphan drug by the European Commission.

Products can be granted orphan drug status because the disease is rare (incidence of less than five in 10 000 people in the European Union) or if developing a treatment for the disease is not commercially viable.³ Active tuberculosis disease is rare in the EU, but as a prophylactic vaccine could potentially be given to everyone our

application was made on the grounds that the vaccine would not generate a sufficient return on investment.

Orphan drug status provides substantial incentives: free scientific advice from the European Agency for the Evaluation of Medicinal Products (EMEA) before registration and at least six years' market exclusivity in the EU once approved. The scientific input should ensure that data on safety, quality, and efficacy are gathered efficiently so that the product can be registered and deployed as quickly and cost effectively as possible.

This is the first time any product has been awarded the designation of orphan drug on the grounds of insufficient return on investment. It is also the first potentially widely deployable prophylactic vaccine to be designated an orphan drug. We have shown that lack of sufficient return on investment offers a potential route for a vaccine or drug being developed specifically for a disease of poverty in developing countries. It is particularly important for prophylactic vaccines where low disease incidence in the EU will not qualify for orphan status.

Vaccines against malaria and HIV are also urgently needed. These vaccines have similar economics and so also require public funding to secure their development. Orphan drug designation could bring the same advantages to such projects. We hope this designation of MVA85A may encourage researchers developing vaccines against these pathogens to consider this route.

T Lang project manager, malaria and TB vaccines trudie.lang@ndm.ox.ac.uk

A V S Hill Wellcome Trust senior principal research scientist

H McShane Wellcome Trust senior clinical fellow Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, University of Oxford, Oxford OX3 7LJ

R Shah *pharmaceutical consultant* Gerrards Cross, Buckinghamshire SL9 7JA

A Towse director C Pritchard health economist M Garau health economist Office of Health Economics, London SW1A 2DY

Competing interests: None declared.

- 1 Datta M, Swaminathan S. Global aspects of tuberculosis in children. *Paediatr Respir Rev* 2001;2:91-6. 2 McShane H, Pathan AA, Sander CR, Keating SM, Gilbert SC, Huygen K, et al. Recombinant modified vaccinia virus
- 2 McShane H, Pathan AA, Sander CR, Keating SM, Gilbert SC, Huygen K, et al. Recombinant modified vaccinia virus Ankara expressing antigen 85A boosts BCG-primed and naturally acquired antimycobacterial immunity in humans. *Nat Med* 2004;10:1240-4.
- European Commission Regulation No 141/2000 of the European parliament of the council of 16 December 1999.

EWTD has negative impact on training for surgeons

EDITOR—Devey expressed concerns about the future of training with the advent of the European Working Time Directive (EWTD) and the modernising medical careers initiative. We have just completed a national survey of 100 senior house officers in ear, nose, and throat medicine to assess the impact of the directive on training.

We found that most of them had their shift pattern changed from an on-call rota (29%) to a partial shift rota (70%). In all, 54% of senior house officers in ear, nose, and throat medicine cross covered other specialties. Sixty three per cent thought that the directive had reduced their training; 31% denied receiving any regular allocated teaching sessions from their seniors. The most important finding was that 71% of these senior house officers were willing to opt out of the directive to safeguard care for patients and their training.

The summary effect of all these changes is to destroy the apprenticeship model of surgical training by separating senior house officer from consultant, and to ensure that ear, nose, and throat patients are cared for, at least partly, by doctors or dentists who have had little or no training in the specialty. To preserve quality of care, and surgical training for the patients of tomorrow we must act now to secure an opt-out for surgeons from the EWTD.

Mohiemen Anwar senior house officer, ear, nose, and throat medicine

dr_mohiemen@hotmail.com

Shabina Irfan senior house officer, ear, nose, and throat medicine

Niall Daly consultant, ear, nose, and throat medicine Furrat Amen specialist registrar, ear, nose, and throat medicine

West Middlesex University Hospital, Isleworth, Middlesex TW7 6AF

Competing interests: None declared.

1 Devey L. Will modernised medical careers produce a better surgeon? *BMJ* 2005;331:1346. (3 December.)

I can fly light aircraft, therefore I can anaesthetise?

EDITOR—I suspect that the reason that commercial pilots and lorry or coach drivers are more regulated than doctors in respect of fitness to perform their duties is that one major mistake kills more people.¹

Strict regulation does not apply to the pilots of light aircraft or gliders carrying passengers. It is up to pilots on a day to day basis to judge their fitness to carry out the complex tasks that flying entails.

It does not seem unreasonable that the same principle should apply to doctors.

Gordon Pledger retired anaesthetist Morpeth, Northumberland NE61 3PN gordonpledger@doctors.org.uk

Competing interests: GP is an ex-anaesthetist and flies light aircraft and gliders.

 $1\,$ Park GR. Am I safe to fly? Am I safe to anaesthetise? BMJ 2005;331:1345. (3 December.)

bmj.com

We select the letters for these pages from the rapid responses posted on bmj.com within five days of publication of the article to which they refer.

Letters are thus an early selection of rapid responses on a particular topic. Readers should consult the website for the full list of responses and any authors' replies, which usually arrive after our selection.