Blood donation, body iron stores, and risk of myocardial infarction - Confidence intervals and possible selection bias call study results into question

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expected, the arrangements for involving local educationalists (clinical tutors, course organisers), and the distribution list for any recommendations made. An independent educationalist should be in attendance during the visits and should make an individual report set against existing educational standards. Assessment of posts needs to be objective and should be seen as such. Subsequent grading of each post as accepted or recommended could be used as an additional incentive for hospitals to improve training, alongside the more draconian measure of withdrawal of funding.

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When midwives perform obstetric tasks at night, trainees can spend more supervised time in clinics
Enrór—Both the survey by Susan Williams and colleagues and the survey by Pamela J Baldwin and colleagues highlighted the need for close support and feedback by senior doctors in order to build the confidence and improve the training of senior house officers. To achieve these goals and ensure appropriate training it is important to recognise the different requirements of career and vocational trainees within a specialty. Most hospitals have accommodated decreased hours by giving junior doctors a day off after a night on call. However, this means that they are likely to miss outpatient clinics or other daytime commitments which represent good training opportunities. Whereas this tradeoff may be acceptable for middle grade staff who need the exposure to on call work, it is probably inappropriate for trainees in general practice.

We reduced the hours worked by trainees in general practice by sending them home after 10:00 pm, rather than by giving them the following day off (during prime training time). This not only improves training but also ensures that staff of at least middle grade review obstetric and gynaecological patients at all times. This is in line with the current expectations of patients and risk management teams.

To facilitate this change we have diverted much work that is traditionally out of hours (e.g. pregnancy assessment, registrar review, and antenatal assessment) to daily clinics, which also provide supervised training opportunities. In addition, we audited bleep calls received by senior house officers at night and found that most were for an assistant at a caesarean section. Therefore, we trained midwives in how to assist. Midwifery training in suturing, cardiocographic interpretation, venesection, and intravenous cannulation was already in place in our unit.

We have now been running the system for more than a year and are pleased to report it is a success. Midwives now undertake all the tasks of obstetric senior house officers at night, with only urgent gynaecological admissions producing extra work for the registrar. This type of admission is rare with our system of daily clinics. An anonymous questionnaire has confirmed that the senior house officers think that their training is better, and the middle grade doctors do not have a significantly higher workload.

We would recommend this system to other similar units, with the one caveat that the number of midwives may need to be increased when the extra pair of hands provided by a senior house officer is removed from the labour ward at night.

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Blood donation, body iron stores, and risk of myocardial infarction
Confidence intervals and possible selection bias call study results into question
Enrór—The importance of stating the 95% confidence interval when reporting results has been shown in a recent paper by Tomi-Pekka Tuomainen and colleagues. In their paper blood donation reduced the risk of myocardial infarction anywhere between 3% and 98%. An estimate with such imprecision seems to be of little use. Moreover, although the association was only marginally significant to begin with (P = 0.047), the authors commented that further adjustments attenuated the association marginally. The confidence interval cannot become considerably wider with further adjustments; even a marginal change at the lower limit of the confidence interval can cause a change in the sign, rendering the association non-significant.

The authors urged that new studies be carried out to confirm their findings. However, although the results of several previous studies were unable to corroborate the hypothesis that raised iron concentrations increase the risk of coronary heart dis-

ease," none of these diverging results was cited in the paper.

Blood donors are not compensated in Finland; they donate blood for altruistic reasons, and evidently such people may also have a great interest in their own health. Thus there was probably substantial selection bias which cannot be adjusted for, especially when only one death was observed among the blood donors. In Finland the study was cited in various news media as firm evidence that blood donation reduces the risk of myocardial infarction. The prestige of the BMJ was used as confirmation of the validity of the study; this seemed ethically questionable to us.

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Authors’ reply
Enrór—We welcome the comments of Harri Hemilä and Mikko Pauino. We have been among the first advocates of the use of confidence intervals when estimates of relative risk are presented in epidemiological studies. Confidence intervals are especially necessary when they are wide—that is, when the sampling variation is large. In our study this was due to the small number of subjects who had donated blood (153 out of 260).

We do not consider P values as important as the strength of the association. In our study, blood donors had as much as an 86% reduction in the risk of acute myocardial infarction after adjustment for risk factors when compared with non-donors. This point estimate did not change much, whichever risk factors we adjusted for. The range of risk factors measured in the Kuopio ischaemic heart disease study is extensive, as shown by our previous publications on the same cohort.

Several studies have concluded that there is no association between iron status and the risk of coronary disease events. All of these negative studies, however, have unreliable measurements of iron status (such as serum iron concentration, transferrin iron saturation) or other design problems, as detailed elsewhere. Comparing the number of positive and negative studies, or the number of subjects in these, seems quite a primitive method from which to derive an overall conclusion. Another reason for not referring to studies using iron status measurements was the lack of space in our short report. A review has been presented earlier.
As we suggested, a randomised blood donation trial in healthy people may be the only possible study design that could ultimately verify or refute a theory about the role of iron balance in coronary disease. There exists a widespread conviction that the more iron in the diet the better. This is what is still written in medical textbooks. This conviction is, however, the enemy of the truth.

We pointed out the potential selection bias in our work—the possibly increased health consciousness of blood donors—and we have repeated this in all interviews given to the media. However, the media tend to simplify issues to make them understandable.

A fundamental problem in all epidemiological studies is that whichever covariates you measure and adjust for statistically, there always remains a possibility that some unmeasured, or too imprecisely measured, confounding factors might explain some of the observed association. We appreciate this, and for this reason our conclusions were cautious and suggested that further clinical trials were needed to resolve the issue conclusively.

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Chaplains on transplant teams facilitate permission being given for organ donation

Ennror—Naomi Craft's news item entitled "Communication increases donor transplant rate" is an interesting example of reinventing the wheel.

Nearly 30 years ago, when I was transplant resident at the Peter Bent Brigham Hospital in Boston, Massachusetts, we routinely saw grieving relatives of brain damaged potential donors, and we were always accompanied by the hospital chaplain. Whenever we did this we were never refused donation of an organ.

When I came back to Charing Cross Hospital I continued the practice, and the chaplaincy became an integral part of the programme. Once again, I do not remember ever having been refused donation of organs when the chaplain participated in the discussion.

I suppose that the grieving relatives felt that the chaplain was on their side rather than mine and was able to clarify this distressing problem.

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Most British research and development in primary care arises outside rural areas

Ennror—What a breath of fresh air to read Mike Pringle's suggestions on improving primary care, which were not exclusively based on the worries of some inner London practices but gave equal consideration to enhancing rural practice. He is prudent to note that innovations need to be evaluated in primary care. I believe, however, that rural developments are at a specific disadvantage compared with urban ones. Almost all the British research and development arises outside rural areas, and so attempts at improvement through evidence based practice have to graft research from urban settings on to countryside problems.

Let me illustrate this with some crude secondary research I did, using papers from last year's Medline (January 1996 to January 1997). This identified 269 items from Family Practice and the British Journal of General Practice, of which 167 seemed to be research papers or short reports. Three of these arose from places in Britain that were not clearly specified (for example, multicentre surveys) and 58 came from outside Britain, but for 106 articles a specific British address was given as the origin of the text. This core British research and development base of 106 papers, 22 papers came from London, 71 from other "cathedral cities" such as Sheffield and Newcastle upon Tyne, and 10 from other urban areas such as Luton and Birkenhead. This left at most three papers that might be described as having arisen from "country towns" (including Cambridge)—less than 3% of the studies.

Research into rural primary care needs to be cultivated. For over two years the Anglian network "Promoting research and development in primary health care" has been doing just that, on a modest scale. Readers interested in the history of NHS innovations may not be surprised to know that the launch of our network in the fens owed a great deal to the foresight and help of an academic in faraway Nottingham—Pringle.

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Amiodarone pulmonary toxicity

Authors did not emphasise typical radiological and histological features sufficiently

Ennror—In their editorial on amiodarone pulmonary toxicity Gillian A J Jessurun and Harry J G M Crijs made some misleading statements about the diagnosis of this dangerous condition. Although they are correct in stating that pulmonary toxicity has rarely been reported after low doses of amiodarone or after short periods of treatment, they make statements relating to the clinical and pathological features that are not supported by the literature or our own experience. They suggest that hyper-inflation is a common radiological manifestation of amiodarone toxicity, that the spirographometric pattern usually suggests obstruction, and that the presence of lamellar inclusion bodies on electron microscopy is specific for amiodarone toxicity. These statements are incorrect and misleading.

The radiological findings in amiodarone lung vary, but the commonest pattern is of asymmetric bilateral alveolar opacification, which may mimic tuberculosis if seen in the upper zones and pulmonary oedema if seen in the midzones and lower zones; other patterns include solitary or multiple masses and lobar or segmental consolidation. Pleural effusions may be seen together with other findings but rarely alone. The radiological differential diagnosis therefore includes infection, heart failure, and malignancy. Computed tomography is more sensitive than plain radiography and may be helpful in distinguishing the appearances from those seen in other conditions; the infiltrate is typically rather dense owing to the presence of iodine. Lung function tests characteristically show a restrictive pattern with reduced diffusing capacity; an obstructive pattern is unusual.

The accumulation of intra-alveolar macrophages seen on cytological examination of bronchoalveolar lavage fluid or on histopathological examination of lung biopsy specimens is not specific for amiodarone; it is also seen in reactions to methotrexate, mitomycin, cyclophosphamide, nitrofurantoin, and bleomycin. Electron microscopy may show lamellated intralysosomal "myelin bodies" because of a direct effect of amiodarone on cellular phospholipases leading to phospholipid accretion. These ultrastructural features may be seen in a variety of diseases, including the phospholipidoses, and reflect exposure to amiodarone rather than toxicity.

The authors give undue prominence to amiodarone pulmonary toxicity presenting as bronchiolitis obliterans organising pneumonia. The number of published case reports of this condition remains in single figures even though eight years have passed since its first description. Bronchiolitis obliterans organising pneumonia is a rare representation of amiodarone pulmonary toxicity, and we would remind readers of the