

children becomes concentrated in large, tertiary paediatric intensive care units.¹ Training junior doctors in more than just the basic skills of resuscitation will be easier in centres with a high throughput of patients, and ultimately this will enable a higher standard of care to be delivered in local hospitals, where most of these doctors will eventually work.

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Premature coronary deaths in Asians

EDITOR,—Sandeep Gupta and colleagues discuss ways in which premature coronary deaths in Asians in Britain might be avoided.¹ When cooking, many people in India and Pakistan use a semisolid fat obtained by partially hydrogenating vegetable oils. This product, called vanaspathi or vegetable ghee, contains high levels of *trans*-fatty acids, which adversely affect blood lipid concentrations and are thus likely to increase the risk of coronary heart disease.²

As part of a pilot investigation conducted at the National Institute of Cardiovascular Diseases in Karachi to assess the feasibility of a case-control study we collected specimens of subcutaneous fat from 48 subjects. The samples were collected by a modification of the technique described by Beynen and Katan,³ stored at 70°C, and transported to the United States on dry ice. Fatty acids were extracted and analysed by capillary gas chromatography with a 100 m column. We found that the 14 subjects who used vegetable ghee for both cooking and frying had significantly higher percentages of *trans*-fatty acids and lower percentages of linoleic and linolenic acid in adipose tissue than the 21 subjects who used only non-hydrogenated vegetable oils (table 1). The adipose tissue of the remaining 13 subjects, who used a combination of different fats, had an intermediate composition.

These data indicate that consumption of vegetable ghee is associated with changes in the fatty acid composition of body fat that are likely to

increase the risk of coronary heart disease. Vegetable ghee is also consumed by south Asians who have settled overseas, and this may help explain their higher mortality from coronary heart disease.^{1,4,5}

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Information about prenatal testing does not necessarily increase uptake

EDITOR,—J G Thornton and colleagues report the effect of giving women extra, non-directive information about prenatal screening.¹ They found that ultrasound examination to look for structural abnormality in the fetus was almost universally accepted (99%) whereas screening for Down's syndrome was accepted by only about one third of the women.

In the first half of a normal pregnancy expectant women are usually offered a scan to enable them and their partner to see their baby, to check the baby's size, or to search for structural abnormality. A search for structural abnormality is not performed until 18-20 weeks, when most of the fetal organs can be assessed. If a woman would like to see her baby but considers abortion to be morally

wrong she can have a scan earlier in pregnancy. This is practical from 12-13 weeks, when the examination is brief and usually includes measurement of the baby's head, which may help the assessment of gestational age.² Additionally, the woman can choose to have a detailed ultrasound examination much later in pregnancy. If a structural abnormality is found at that stage she will be cared for jointly by a consultant obstetrician and a consultant neonatal paediatrician.

It is unclear if this information was available to the women in the authors' study before the first antenatal visit, an occasion when women face information overload.¹ Most women are aware of screening for Down's syndrome before they become pregnant and may have preconceived attitudes towards it; they are usually unaware of the scope of ultrasonography at different gestational ages in the first half of pregnancy.

I share the authors' suspicion that many women choose screening if to do so is perceived as normal. Experience has taught me, however, that uptake of screening for fetal structural abnormality at 18-20 weeks is less than 99% when women and their partners have had the opportunity to consider choices in ultrasonography before the first antenatal visit.

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One and two view mammography in breast cancer

Are carcinomas detected by one and two view mammography similar?

EDITOR,—Nicholas Wald and colleagues detected 24% more carcinomas with two view mammography than with one view mammography in the prevalence round of breast cancer screening, and they recommend that two view mammography should be standard practice.¹ They calculate the potential effect of this on mortality. Implicit in such calculations is the assumption that the behaviour of the carcinomas detected only by two view mammography is the same as that of the carcinomas detected by one view mammography.

The proportion of carcinomas that were invasive (rather than purely in situ) and 10 mm or less in diameter was similar in patients who had only one view mammography and patients who had only two view mammography. No comment is made about the pathology of carcinomas in patients who had two view mammography with one view interpreted by one radiologist and both views by another—which allows comparison of carcinomas detected only by two view mammography with the carcinomas detected by one view mammography.

For invasive carcinomas, standard pathological prognostic factors would be useful: tumour size, histological grade, histological type, and axillary nodal status. Although prognostic factors are less well defined for in situ carcinoma, the size, type, architecture, and grade or differentiation would be of interest. The study by Wald and colleagues has major implications for breast cancer screening. Ideally, carcinomas detected by one and by two view mammography would be compared with survival analysis, but this would require an enormous number of patients and long follow up. Pathology has been used as a surrogate marker in the assessment of breast cancer screening programmes. Full pathological details of all three

Table 1—Comparison of content of adipose tissue (expressed as percentages) in 48 subjects according to type of fat used for cooking and frying. * Figures are means (SD)

| | Type of fat | | |
|---------------------------------|--------------------------|--|--------------------|
| | Vegetable ghee (n=14) | Non-hydrogenated vegetable oil (n=21) | P value (ttest) |
| Saturated fatty acids | 26.89 (4.34) | 26.34 (4.75) | 0.73 |
| Cis-monounsaturated fatty acids | 43.99 (5.08) | 40.86 (8.40) | 0.22 |
| Oleic | 37.62 (3.53) | 34.37 (8.66) | 0.14 |
| Cis-polyunsaturated fatty acids | 16.03 (5.07) | 21.61 (6.34) | 0.01 |
| Linoleic 18:2n-6 | 13.74 (4.90) | 18.68 (5.65) | 0.01 |
| Linolenic 18:3n-3 | 0.60 (0.22) | 1.07 (0.80) | 0.02 |
| Dihomogamma linolenic 18:3n-6 | 0.25 (0.08) | 0.30 (0.11) | 0.11 |
| Arachidonic 20:4n-6 | 0.55 (0.30) | 0.48 (0.19) | 0.40 |
| Long chain n-3 fatty acids | 0.36 (0.11) | 0.45 (0.20) | 0.11 |
| 20:5 | 0.07 (0.06) | 0.07 (0.05) | 0.93 |
| 22:5 | 0.18 (0.07) | 0.22 (0.09) | 0.18 |
| 22:6 | 0.11 (0.06) | 0.16 (0.09) | 0.11 |
| Total <i>trans</i> -fatty acids | 4.99 (1.82) | 3.41 (1.75) | 0.01 |
| Total 18:1 <i>trans</i> | 3.92 (1.60) | 2.65 (1.60) | 0.03 |
| Total 18:2 <i>trans</i> | 0.96 (0.36) | 0.63 (0.40) | 0.02 |
| <i>Trans, trans</i> 18:2n-6 | 0.13 (0.11) | 0.13 (0.11) | 0.83 |
| <i>Cis-9, trans-12</i> 18:2n-6 | 0.59 (0.23) | 0.33 (0.25) | 0.005 |
| <i>Trans-9, cis-12</i> 17:2n-6 | 0.24 (0.12) | 0.17 (0.21) | 0.26 |

*Thirteen subjects used a combination of fats.

groups in Wald and colleague's study would be useful.

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Many subjects in trial were not asked for consent

In the UKCCCR multicentre randomised controlled trial of one and two view mammography in breast cancer screening, only one out of the nine breast screening centres that took part sought informed consent before randomisation from the 40 163 women attending their first breast screening examination who participated in this trial.¹ The remainder sought consent after randomisation and only from those women who had been allocated to either of the two view arms (ratio 1:1:2)—that is, a quarter of the women in eight out of nine centres did not know they were in a trial.

Might it be assumed that the trial working party decided this because consent is not sought from women "invited" for breast screening? Presumably it was deemed to be unjust to those millions of women who have attended for mammographic screening without benefit of the provision of adequate balanced information that informed consent would confer. Should we not now be asking if it was unjust and unethical for those women in this trial not asked for consent, particularly as the stated conclusion that "two view mammography is medically more effective than one view: it detects more cancers and reduces recall rates; it is also similarly cost effective financially" could hardly be said to be counter intuitive?²⁻⁵

Is it not time that all women who attend for screening are presented with proper, balanced information and asked for consent? It would be particularly interesting to know the opinion of the 9000 or so unsuspecting women who unknowingly participated in this trial. Such better informed women would be better placed to enter into the debate concerning the value (economically and psychologically) of screening in terms of reducing the morbidity and mortality of women with breast cancer.

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Redefining marginal costs and benefits

EDITOR,—The results of the study by Nicholas Wald and colleagues¹ indicate that two view mammography is more effective in detecting breast cancers than a single view technique, but as it is more expensive there is little difference in average costs per cancer detected by these two

methods. The "marginal" cost of two view screening has been taken to be the difference in average screening costs divided by the difference in the number of cancers detected by each method. In the context of this study, the marginal benefits of two view mammography are the extra cancers detected and the marginal costs are the extra expenditures incurred in their detection. Thus the true marginal cost of the two view method is the difference in total costs of the techniques divided by the difference in the number of cancers detected.

Furthermore, although costs are incurred at the time of screening, benefits (years of life saved) accrue over several years. The authors might therefore have considered the process of discounting in their calculation of costs per year of life saved.

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High detection rates do not necessarily lead to lower mortality

EDITOR,—The finding of a substantially higher rate of detection of breast cancer by two view compared with single view x ray mammography in the well designed randomised clinical trial by Nicholas Wald and colleagues deserves comment.¹ The assumption in the authors' four key messages that high detection rates will lead to larger reductions in mortality from breast cancer is not borne out by evidence from the randomised controlled trials summarised by Fletcher *et al.*² The Health Insurance Plan trial detected 2.7 cancers, the Malmö trial 7.5 cancers, and the Edinburgh trial 6.2 cancers per 1000 women, but as the reduction in mortality produced was 29%, 19%, and 16%, respectively, the higher detection rate did not lead to the most favourable outcome in terms of reduced mortality.

Benefits of a screening programme rest on other factors also, including diagnosis and treatment. Britain does not have the highest incidence of breast cancer but has the highest mortality from the disease. It seems that life expectancy can be extended only in a proportion of cases. On the other hand, some detected cancers will never become life threatening if left alone.

The 24% increase in detection implies that the sensitivity (with one view as used until recently in screening in Britain) has been at best 76%; this is also consistent with the report of unexpectedly high rates of interval cancers (82% of the underlying incidence) in the third year after the start of the screening programme in Britain. Two view mammography is reported to miss 16.5% of palpable cancers; we therefore estimate that the overall sensitivity of the British programme to date will have been about 65%. Thus 35% of women with cancer who accepted an invitation to screening have been given false reassurances. This will have led to delays in management of some women with invasive disease.

The fact that these trial results have appeared some seven years after the inception of the screening programme supports the views of Skrabanek, Jatoti and Baum, and Rodgers that women should be given the fullest possible information on the uncertain balance between risks and benefits of the screening and then, if they agree, sign a consent form.^{3,4} Even if the basic hypothesis of screening—that early detection leads to increased expectancy for a small subset of those screened—is correct, the results of this study into the methodology of mammographic screening, together with the

problem of overdiagnosis and consequent over-treatment, show that the British programme is in effect a large scale trial operating in virtually uncharted waters.

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Authors' reply

EDITOR,—As A H S Lee and colleagues imply, cancers detected only by two view mammography would be expected to be smaller, but our data indicate that any difference is small. Tumour size was similar in women who had either one or two views. In the group which had two views (one interpreted by one reader and both by another) the median size of the tumours detected by one view only was 13 mm compared with 12 mm if two views were used.

The effectiveness of breast cancer screening has been well demonstrated in randomised trials, and our trial shows the advantage of two view mammography over one view. To perform a trial of two view mammography with mortality from breast cancer as the end point would be impractical and unnecessary. As randomised trials have shown that mammographic screening reduces mortality, the prevalence of cancer detected by screening is a sufficient end point in trials comparing screening methods. If two view mammography detects 24% more preclinical cancers than one view, given the evidence on tumour size, a similar proportionate effect on mortality would be expected. The absence of a simple relation between the prevalence of detected cancers and the proportionate reduction in mortality from breast cancer across different trials of screening confirms that the rates of breast cancer and the effect of treatment vary in different populations and at different ages. It does not mean that the effectiveness of screening in detecting cancers is unrelated to its effect in reducing mortality.

It is reasonable to seek consent to participate in research from individuals invited to have a treatment or procedure that departs from recommended practice. Because one view mammography was recommended practice, consent was obtained only from women receiving two views. This issue is unrelated to that of providing appropriate information to women attending for screening, which should be (and was) done routinely.

Sneh Bhargava and colleagues have misunderstood our economic calculations on the marginal cost of two view mammography. This was done in the standard way (the difference in total costs between one and two view mammography divided by the number of extra cancers detected) with the total costs based on the average costs of screening women by each method. The costs related to detecting a cancer at the time of screening, so