Follow up in breast cancer

Quality of life unaffected by general practice follow up

EDITOR,—John Dewar calls for a reappraisal of how women with breast cancer are followed up.¹ We now have compelling evidence that intensive follow up does not improve either quality of life related to health or overall survival.^{2,3} In the light of this, Dewar wonders what the effect of routine follow up is on the patient, in terms of both quality of life and cost. He also wonders what the optimum follow up practice should be and calls for as rigorous an assessment of follow up practices as has been applied to screening practices. An important step in that direction was the consensus conference on follow up in breast cancer, which he cites.

Among the papers presented at that conference was one giving the interim results of a randomised controlled trial we recently conducted.⁴ This trial evaluated a system of routine follow up that is centred on general practice rather than on specialists, as is the current standard practice. Patients were randomised to routine follow up by their own general practitioner or to continue routine follow up in specialist clinics. We monitored the quality of life of patients in both arms of the trial. At mid-trial there were no differences between the two groups. The fact that two thirds of eligible patients agreed to participate in the trial suggests that patients are willing to consider follow up by their general practitioner as an alternative to hospital follow up if given the choice. In addition, it suggests that a proportion of patients will choose to continue with hospital follow up. This will ensure that a proportion of patients seen in clinics are "fit": Dewar notes that such patients are an important counterbalance to the many seriously ill patients seen in these clinics. We also found that general practitioners were willing to provide follow up: 113 of the 115 general practitioners with patients in the trial agreed to provide follow up care. This is further supported by a separate survey of general practitioners in which 69% selected routine follow up by the general practitioner as their preferred method of follow up.⁵

We embarked on this trial out of concern for the many issues that Dewar raises. We decided to evaluate a system of follow up centred on general practice because we thought that it would address many of these issues and, at the same time, ensure continuity care and support for the patient. We believe that this is the ideal method of shared care: the specialist provides primary treatment, the

general practitioner provides continuing care, and the specialist becomes involved again if disease recurs.

EVA GRUNFELD
Assistant professor

Department of Medicine,
University of Ottawa,
Ottawa,
Ontario,
Canada K1H 8L6

PAT YUDKIN
Statistician, ICRF General Practice
Research Group

RUTH ADEWUYI-DALTON
Research assistant

MARTIN P VESSEY
Professor of public health and
primary care

Department of Public Health and Primary Care,
University of Oxford,
Oxford OX2 6HE

DAVID MANT
Professor of primary care
epidemiology

Department of Primary Medical Care,
University of Southampton,
Southampton SO1 6ST

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Patients prefer specialist follow up

EDITOR,—We wish to report the "missing data"—namely, patients' views—in the debate on routine follow up in breast cancer.¹ As part of the design process for a multicentre study of hospital follow up versus follow up based in the community we sought patients' views using research methods described by the College of Health.² Focus groups of women in remission were drawn both randomly and from the network of cancer support groups established around Mount Vernon Cancer Centre.³ The focus groups discussed alternatives to the present system of follow up.⁴ The patients' view challenges the utilitarian approach of clinicians, and shows differences in the perception of the purpose of routine follow up in the two communities.

The patients expressed their anger and distress about being discharged to their general practitioners for follow up without having the support and specialist services of the hospital available in the community. They challenged the researchers' hypothesis; patients viewed the hospital—its diagnostic tests, specialist physicians, and breast care nurses—as their best defence against a recurrence of their cancer. The hospital was seen as having skill in cancer and understanding the magnitude of cancer in the patients' life. Although there were aspects of the hospital system they did not like—the waiting, the rushed consultations, and the lack of continuity of care—these were seen as the trade off for guarding against a relapse. While there is

no evidence that routine follow up improves prognosis or reduces rates of recurrence, this was not the message they had received.

For patients, an acceptable model of community based care would include clinics staffed by someone with specialised knowledge of cancer—for example, a breast care nurse—and a fast track route back to hospital care when this is required; this would overcome the perceived lack of knowledge of their special needs by general practitioners and provide continuity and a specialised intermediate service. Hospital specialists would also have a reduced workload, allowing them to concentrate their care on those who really need it.

While other models may be proposed, at a time when cancer services are primed for reorganisation (precipitated by the Calman report) the views of the patients should not be ignored. Frequently we have found that patients, with their wealth of experiential knowledge, can suggest solutions when clinicians cannot see the wood for the trees.

JANE MAHER
Clinical director

JANE BRADBURN
Researcher

RUTH ADEWUYI-DALTON
Research assistant

Lynda Jackson Macmillan Cancer Support and
Information Centre,
Mount Vernon Hospital,
Northwood,
Middlesex HA6 2RN

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Impossible to state which NSAID is safer

EDITOR,—In their article on recent advances in rheumatology Anthony Bradlow and Joel David state that ibuprofen is the safest non-steroidal anti-inflammatory drug when used at conventional doses.¹ However, they present only the risk of serious gastrointestinal adverse events and these for only the seven most commonly prescribed non-steroidal anti-inflammatory drugs.

Data from the Medicines Control Agency show that the incidence of hypersensitivity reactions associated with ibuprofen is similar to that of gastrointestinal reactions (0.5-1 report per 100 000 prescriptions).² Both ketoprofen and indomethacin are less likely to provoke hypersensitivity reactions. Spanish data collected in a similar manner show that only 39% of adverse events associated with non-steroidal anti-inflammatory drugs were gastrointestinal.³ Gastrointestinal adverse reactions are considered to depend on the dose.⁴ It is difficult to assess, from data reported voluntarily or observationally, whether the dose was equivalent between these non-steroidal anti-inflammatory drugs.

For various reasons, different non-steroidal anti-inflammatory drugs are used for different indications. This leads to them being used in different

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populations, with variable doses and durations, which creates further difficulty in interpreting such data. We therefore conclude that it is not possible to state with certainty which of the seven most commonly prescribed non-steroidal anti-inflammatory drugs is the safest; six of these seven have similar profiles of adverse events.

STEPHEN REVELL
Pharmaceutical physician
F Hoffman-La Roche,
Drug Safety,
CH-4002 Basle, Switzerland

LINDA FENNEY
Pharmaceutical physician
F Hoffman-La Roche,
Drug Safety,
Palo Alto, USA

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Antidepressants and suicide

Study analyses were flawed

EDITOR,—Two recent articles look at use of antidepressants and death from suicide. John A Henry and colleagues have continued previous work and assessed the relation between death and defined daily dose.¹ Unfortunately, the defined daily dose for dothiepin used in the paper (75 mg) should be 150 mg (references quoted by Henry and colleagues). The correct figure is then 3.08 deaths per million defined daily doses of dothiepin instead of 1.54—the second highest figure, after that for amoxapine. This agrees with a clinical study that showed that dothiepin has greater toxicity in overdose than other tricyclic antidepressants.² We are also concerned about the statistical methods used by Henry and colleagues. It is unclear how valid confidence limits are in this context without a clear definition of x and how the standard error (not deviation) was calculated. It is inappropriate to use one tailed tests of significance without a prior hypothesis, and it is incorrect to use Fisher's exact test to compare rates.

In the study by Susan S Jick and colleagues we question the inclusion of flupenthixol, which is more likely to be used for schizophrenia than depression and is usually used as a depot preparation.³ Also, the overall suicide rate of 8.3 per 10 000 person years of antidepressant use seems remarkably low and is much lower than rates in affective disorder cited in the literature.⁴ The data from Henry and colleagues' paper give a death rate for poisoning with dothiepin alone of 11.25 per 10 000 person years of use.¹ These discrepancies raise three possibilities. One is that prescribers were using antidepressants mainly for conditions other than affective disorder. Another is that suicide was considerably underestimated in the cohort. In Henry and colleagues' study only 56% of the deaths due to poisoning were suicides, the remainder being undetermined. To ignore these deaths when comparing outcome may obscure differences in toxicity between antidepressants in overdose. Thirdly, there was systematic underdosing of the antidepressants in the study compared with the defined daily dose. Obviously, combinations of all three factors may have occurred.

Finally, Jick and colleagues comment that their data are consistent with the proposition that those who are determined to commit suicide will find a way that produces the intended outcome. This

comment would be supported only if they could show that patients on their database who survived self poisoning went on to commit suicide by other means. This is not supported by the literature, which indicates that most patients who survive after taking an overdose do not subsequently kill themselves by other means.⁵

IAN WHYTE
Senior staff specialist
NICK BUCKLEY
Senior lecturer
GREG CARTER
Senior staff specialist
Department of Clinical Toxicology and Pharmacology,
Hunter Area Health Service,
Newcastle Mater Misericordiae Hospital,
Locked Bag 7, Hunter Regional Mail Centre,
NSW 2310, Australia

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Study is based on unproved assumptions

EDITOR,—John A Henry and colleagues draw several familiar conclusions from their study of suicide and antidepressants.¹ They argue that their data "provide a useful guide to the relative toxicities of drugs and an indication of the needs for prescribing policy" and suggest that a considerable number of suicides could be prevented by a switch to routine prescribing of selective serotonin reuptake inhibitors. This opinion is not always expressed in such restrained terms—as the accompanying editorial reminds us²—and yet it is based on two unproved assumptions. The first is that relative mortality due to overdose is the same as relative toxicity in overdose. The second is that suicidal patients prescribed a non-toxic drug will not seek an alternative means of killing themselves.

Since the data on relative mortality due to an overdose of antidepressants do not come from randomised trials they could reflect differences between patients prescribed different antidepressants rather than differences between the drugs themselves. There is evidence to support this interpretation. For example, when Farmer and Pinder derived a similar "toxicity" index using data from Intercontinental Medical Statistics they found that for each antidepressant the index was lower in those aged over 65 than in younger people³; this cannot be reconciled with the suggestion that the index reflects cardiotoxicity in overdose. If the index measures drug toxicity then it should be stable over time; in fact, the index for amitriptyline calculated for the years 1975-84 is 46.5 (95% confidence interval 43.9 to 49.1)⁴ and for the years 1987-92 is 38.9 (35.6 to 42.4).⁵

If antidepressants do differ in toxicity in overdose it does not follow that routine prescribing of drugs with lower toxicity will reduce the suicide rate. Such a conclusion would be justified only if there was no substitution of method—in other words, if the prescription of a more toxic drug offered an opportunity for suicide that the depressed person would not find elsewhere. The study by Susan S Jick and colleagues substantially undermines this "loaded gun" argument against the tricyclic drugs since its main finding is that prescription of an older tricyclic antidepressant (rather than a new drug) does not constitute a risk factor for suicide.⁶

Contrary to the conclusions of this paper, there

is uncertainty about the true difference in toxicity of different antidepressants in overdose and about the effect of substitution of method in a suicide prevention strategy based on prescribing policy. The small number of lives that might potentially be saved by prescribing the selective serotonin reuptake inhibitors must be set against the costs. Our cost effectiveness study showed how expensive such a prescribing policy might be when compared with other public health policies,⁶ even when the calculations were based on assumptions compatible with the data presented by Henry and colleagues. These latest studies do nothing to challenge our conclusion that a widespread move to prescribing specific serotonin reuptake inhibitors as first line treatment for depression cannot be justified on the evidence available.

ALLAN HOUSE
Consultant
Department of Liaison Psychiatry,
Leeds General Infirmary,
Leeds LS1 3EX

TREVOR SHELDON
Director
NHS Centre for Reviews and Dissemination,
University of York YO1 5DD

NICK FREEMANTLE
Research fellow
Centre for Health Economics,
University of York,
York YO1 5DD

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Study did not consider treatment efficacy

EDITOR,—The papers on suicide and antidepressants in the issue of 28 January develop our understanding of this problem further. John A Henry and colleagues point out the differences in the rate of death by overdose for different antidepressants¹ but fail to relate this to efficacy and the fact that only 4-5% of all suicides are due to an overdose of antidepressant.² Susan S Jick and colleagues show that many people taking antidepressants commit suicide but do not give data on the number of suicides that occur in untreated depressed patients.³ Interestingly, they found a distinct difference in crude rates of suicide between people taking tricyclic antidepressants (7.4 (range 4.7-8.7) suicides/10 000 person years) and people taking non-tricyclic antidepressants (flupenthixol, mianserin, fluoxetine, or trazodone; 14.9 (12.0-19.0) suicides/10 000 person years). The further analyses of fluoxetine, the antidepressant with the highest crude rate of suicide (19.0/10 000 person years), suggested that this rate could partly be explained by selection bias, in particular related to "history of suicidal behaviour." There seemed, however, to be "residual factors which reflected a higher risk of suicide for subjects taking fluoxetine."

Evidence suggests that the selective serotonin reuptake inhibitors (such as fluoxetine) are less effective than the tricyclic antidepressants, particularly in the more severe melancholic type of depression.⁴ If patients with this type of depression constitute an appreciable proportion of those at risk of committing suicide then the earlier recommendations, based on data on the toxicity of drugs in overdose, that the tricyclic antidepressants should be abandoned may have contributed to an increase in the overall rate of suicide. As was pointed out in a similar debate a year ago, the