

EDITORIAL

Depression undertreatment: lost cohorts, lost opportunities?¹

Depression is in the news! In this country the Defeat Depression Campaign (Royal College of Psychiatrists, 1993) launched by the Royal Colleges of Psychiatrists and of General Practitioners is both consensus driven and media directed; to this may be added the emergence of consensus statements on depression treatment elsewhere in the world. Suicide reduction as a national health outcome target (Department of Health, 1992), in part through the more effective treatment of mental illness and particularly depression, is further evidence of a growing interest in this topic outside psychiatry.

Apart from the enormous disability and economic cost of depression, its well established treatability makes it a priority topic for attention in any public health strategy programme that aims to deliver efficiency (financial) as well as efficacy (clinical, social and economic functioning). The welter of evidence from randomized control trials (RCTs) and other relevant data on efficacy has recently been digested by multidisciplinary groups given the task of achieving consensus statements on management. Clearer guidelines have emerged on what clinicians should do (Paykel & Priest, 1992; American Psychiatric Association, 1993; British Association for Psychopharmacology, 1993) in order to make depressed patients better (recovery, remission), to remain better (continuation and recurrence prevention), to avoid a future relapse (maintenance or new episode prevention), and on how to manage a failure to respond (Depression Guideline Panel, 1993). If the desired targets are to be achieved, the question that public health physicians must ask and which epidemiologists should be able to answer is 'Does existing treatment also work as well as one would expect in routine clinical practice in the "real" world?'

The following fictitious conversation may serve to illustrate the question. A psychiatrist and an epidemiologist, formerly undergraduate students together, chancing upon one another on the train and both travelling to their respective national advisory committees soon engage in conversation about psychiatric claims for obviously realizable public health gains. There is a debilitating condition (major depression) affecting approximately 5% of the adult population; a choice of treatment options, relatively inexpensive (indeed free in most industrialized countries), increasingly safe, and if necessary with very simple instructions (take one when going to bed); and in RCTs treatment typically increases the recovery rate after 4–6 weeks from 1/3 to 2/3 of cases. The epidemiologist then asks: 'How much has the prevalence fallen since treatments became widely available?'. The psychiatrist, pausing for a moment, points out there are problems: poor case detection (an important but separate issue), high relapse rates and difficulties with achieving consistent prevalence estimation. But even allowing for these, it would be hard to say that prevalence has been noticeably reduced. The epidemiologist acknowledges that the incidence could be rising for other reasons and any secular trends may be too gradual for an effect to be detectable, so what evidence is there from prospective cohort surveys and data base records of routine practice that those treated have a better outcome than the untreated, as you would expect? The topic of conversation drifts elsewhere, the psychiatrist vowing to chase up the literature on that....

It is clear that retrospectively identified cohorts may be unreliable because patients who 'dropped out' following a decision to treat depression may fail to be identified and included. Reports from treatment services will have to be judged on how well they describe outcome in relation to the total pool of referrals originally received; *ad hoc* follow-up studies of subjects originally enrolled in

¹ Address for correspondence: Dr T. S. Brugha, Department of Psychiatry, University of Leicester, Clinical Sciences Building, Leicester Royal Infirmary, PO Box 65, Leicester LE2 7LX.

RCTs, such as those designed to compare drug and psychotherapeutic treatment modalities (Shea *et al.* 1992), may not be representative of 'standard' clinical practice; whereas representative samples identified, or verified, through population-based psychiatric case registers (unless funding was withdrawn) and comparable systematically maintained patient databases could be extremely helpful. Nosocomial factors are important; community, primary health care, out- and in-patient series should be distinguished.

Published, prospective studies of subjects with depressive symptoms exist in considerable numbers, but studies that take clinical management into account are surprisingly difficult to find even among patients in contact with specialized psychiatric services. A recent monograph on prediction in *Psychopharmacology* (Abou-Saleh & Filip, 1993) provided data on factors that influence response to treatment in a variety of disorders; but observational data that predict outcome in relation to a decision to commence or alter treatment of depression appeared difficult to locate. In the same monograph, a review of 44 studies on predication in psychiatry and psychopharmacology (Hoschl, 1993), of which 13 appeared related to depression or suicide, showed only one study in which a treatment predictor (ECT) was considered. Of those cohort studies cited in a recent practice guideline, hardly any were designed to compare treatment effects on outcome (American Psychiatric Association, 1993). Thus, surprisingly little is known of the effectiveness of specialized psychiatric services in the management of depression (Kupfer & Freedman, 1986; Glick *et al.* 1991).

Two long-term outcome studies based on in-patients treated by specialized services paint a dismal picture: (Kiloh *et al.* 1988; Lee & Murray, 1988). As Kiloh and colleagues (1988) commented in their report of 133 patients with at least one admission for primary depressive illness, followed up after typically 15 years during which only 20% had remained continuously well: 'the profession is confident about the management of acute episodes of depressive illness and of treatment-resistant chronic depression... in the present data few factors, apart from prior hospital admission, seem to be of prognostic import'. And in the report from Lee & Murray (1988) on a smaller, similar series identified at first admission, 'good immediate response to treatment may offer false hope...'; patients with illnesses that were classified as less neurotic and more bipolar (or endogenous) in form 'were eventually found to have very poor outcomes, despite apparently good immediate responses to physical treatments'. Shorter-term follow-ups from treatment trials (RCTs) also show poor (sustained) recovery rates and high relapse rates (Shea *et al.* 1992).

Two groups of workers have employed the prospective cohort method in an attempt to study the relationship between depression and its treatment and later outcome. Both reveal evidence of the under-use of effective treatments by psychiatrists in well-resourced centres (Keller *et al.* 1986; Brugha & Bebbington 1992; Brugha *et al.* 1992). From studies on the course of episodes of depression carried out at the MRC Social Psychiatry Research Unit in London, 51% of a cohort of 119 depressives, mostly out-patients, were no longer cases on the PSE Index of Definition (Wing *et al.* 1990) when assessed at follow-up, 3–6 months after their initial contact with services. Of those not yet recovered, it was judged that only 13 patients (22%) were offered an alternative, potentially effective form of care such as admission, day care, psychotherapy referral, change of drug regime (Brugha & Bebbington, 1992). Most of these patients had not been discharged back to their general practitioner. Thus, it would appear that 39% of this group of prospectively assessed patients were being denied a form of treatment from which they had an ability to benefit. Drug treatment was unrelated to outcome at follow-up, even when dosage, compliance and possible influences on treatment selection, such as initial severity, were taken into account. Similarly, Keller *et al.* (1986), in a prospective study of 338 patients with major depression (74% were admitted), in the NIMH Collaborative Program on the Psychobiology of Depression, clearly documented substantial failure to utilize both drug and psychotherapy treatments of well-established efficacy in non-recovered patients. Lack of treatment was not clearly explained by nature or severity of illness, but rather by differences between clinicians. They also commented that the maximum level of treatment received (i.e. ECT, drug treatment that took account of dosage, psychotherapy) during any 4-week block, in the first 8 weeks after intake, revealed no substantial differences in cohorts who had a rapid

recovery compared with patients who remained severely ill (Keller *et al.* 1986). In a recent more detailed report on the cohort, now enlarged to 431 subjects (Keller *et al.* 1992), they showed that at 8 weeks follow-up, 69% of patients had not yet recovered and the level of treatment activity was in decline, somatic treatments having achieved a peak at 4–6 weeks; an association between intensity of treatment and decline in symptoms could only be demonstrated in the initial 6-week period of more active somatic treatment. Both research groups were quick to acknowledge that observational data, even when gathered prospectively, cannot be compared with experimental (RCT) data for demonstrating objective, scientific proof of the efficacy of an intervention. How well a treatment works is not the issue; rather, why does the existence of efficacious measures not produce expected health gains in a defined population across the full range of patients for whom it is intended? Both studies clearly document lost opportunities except perhaps in the first few weeks after treatment was started. Beyond that, patients did not appear to receive appropriate treatments, justifiable changes of treatment, or treatment alternatives from which they could benefit, and outcome was poor. Although both studies were completed before the more recent widespread adoption of safer non-tricyclic (SSRI) drug treatments, what evidence is there that their introduction has resolved the issue?

What should we do now? It is timely that the assessment of medical effectiveness (*Cross Design Synthesis*, 1992) and of the effects of health technologies (NHS Management Executive, 1992) has come under government scrutiny on both sides of the Atlantic also. Both bodies of experts repeat the call for randomized trials and for analyses of observational data but differ somewhat in their advice on the benefits and disadvantages of each. The much more detailed report to Congressional Requesters (*Cross Design Synthesis*, 1992) acknowledges the problem that the results of randomized trials may not be applicable to actual medical practice; it goes on to deal extensively with the methods available for overcoming the problem of imbalanced comparison groups in observational studies in which patients are not randomly assigned to alternative treatments. Their concluding recommendation is for a strategy that extends the logic of meta-analysis, combining results from studies that have different, complementary designs and, hence, the development of what they term Cross Design Synthesis.

The Clinical Practice Guidelines in the USA and the Defeat Depression Campaign and comparable efforts to alert those who could act more effectively are clearly welcome. But do we know enough yet about how much under-treatment there is and why? The two cohorts discussed here were not primarily recruited in order to answer such questions and may not be relied upon for general explanations for the poor outcomes that they clearly demonstrate. Although knowledge of what is efficacious is constantly changing, the existence of practice guidelines now provides an important opportunity to count our successes and failures. A clear consensus now exists on what to do about initial intervention (assessment of possible causes, treatment choice and availability, safe prescribing, education of patient and family, monitoring of good, inadequate and adverse outcomes, specialist referral), treatment failure, recovery maintenance and relapse prevention (Depression Guideline Panel, 1993). Failure of initial treatment, recovery maintenance and relapse prevention probably require the greatest attention in such work. It is now possible for us to classify the reasons for, and therefore reliably to enumerate undertreatment in future, representative cohorts, by using prospectively gathered data both from patients and from those treating them. Only prospective assessments that begin at the time of the initial diagnostic assessment, which also include reliable, contemporaneous data on treatment and compliance, can be fully relied upon (Brugha & Bebbington, 1992).

Only when we know 'why' and 'how much', will it be possible to devise, and reliably assess, strategies to reduce undertreatment, by conducting randomized studies that avoid as far as possible the artificial conditions that may make existing randomized trials insufficiently representative. Thus, if the cause of undertreatment lies in some aspect of professional practice, treaters rather than patients would be randomized to receive interventions in the form of training packages, routine audits and peer reviews, (Stocking, 1992) which make use of feedback of standardized measures of subsequent health status (outcome?). In effect, trials would be more like routine practice because

those treated would be more representative, but equally, routine treatment might be more like practice within trials, with greater, systematic attention to evaluation, compliance management and pursuit of non-attenders. There is already encouraging evidence of the beneficial effects of locally introduced clinical guidelines into medical practice (Grimshaw & Russell, 1993). The longer term durability of successful interventions may also have to be tested.

National and local research and development strategies are also in the news. Research priorities have been set and no doubt will be reviewed. Experts in health technology assessment and the transfer of clinical research findings, public health medicine, epidemiology, clinical psychology and psychiatry who are contributing to that process, please take note! There may be an opportunity here that we cannot afford to miss if we hope for more of our patients to survive us.

T. S. BRUGHA

REFERENCES

- Abou-Saleh, M. T. & Filip, V. (1993). Prediction in psychopharmacology. *British Journal of Psychiatry* **163** (Suppl. 21).
- American Psychiatric Association, (1993). *Practice Guidelines for Major Depressive Disorders in Adults*. American Psychiatric Association: Washington, DC.
- British Association for Psychopharmacology (1993). Guidelines for treating depressive illness with antidepressants. *Journal of Psychopharmacology* **7**, 19–23.
- Brugha, T. S. & Bebbington, P. E. (1992). The undertreatment of depression. *European Archives of Psychiatry and Clinical Neuroscience* **242**, 103–108.
- Brugha, T. S., Bebbington, P. E., MacCarthy, B., Sturt, E. & Wykes, T. (1992). Antidepressives may not work in practice: a naturalistic prospective survey. *Acta Psychiatrica Scandinavica* **86**, 5–11.
- Cross Design Synthesis: A New Strategy for Medical Effectiveness Research (1992). Report No. B244808. US GAO: Washington DC.
- Department of Health (1992). *The Health of the Nation*. (CM 1523.) HMSO: London.
- Depression Guideline Panel (1993). *Depression in Primary Care: Volume 2. Treatment of Major Depression*. Clinical Practice Guideline Number 5. Rockville MD, US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research. AHCPR Publication No. 93-0551.
- Glick, I. D., Burti, L., Suzuki, K. & Sack, M. (1991). Effectiveness in psychiatric care. I. A cross-national study of the process of treatment and outcomes of major depressive disorder. *Journal of Nervous and Mental Disease* **179**, 55–63.
- Grimshaw, J. M. & Russell, I. T. (1993). Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet*, **342**, 1317–1322.
- Höschl, C. (1993). Prediction: nonsense or hope? *British Journal of Psychopharmacology* **163** (Suppl. 21), 46–54.
- Keller, M. B., Lavori, P. W., Klerman, G. L., Andreason, N. C., Endicott, J. & Coryell, W. (1986). Low levels and lack of predictors of somato-therapy and psychotherapy received by depressed patients. *Archives of General Psychiatry* **43**, 458–466.
- Keller, M. B., Lavori, P. W., Mueller, T. I., Endicott, J., Coryell, W., Hirschfeld, R. M. A. & Shea, T. (1992). Time to recovery, chronically, and levels of psychopathology in major depression. *Archives of General Psychiatry*, **49**, 809–816.
- Kiloh, L. G., Andrews, G. & Neilson, M. (1988). The long-term outcome of depressive illness. *British Journal of Psychiatry*, **153**, 752–757.
- Kupfer, D. J. & Freedman, D. X. (1986). Treatment for depression. 'Standard' clinical practice as an unexamined topic. *Archives of General Psychiatry* **43**, 509–511.
- Lee, A. S. & Murray, R. M. (1988). The long-term outcome of Maudsley depressives. *British Journal of Psychiatry* **153**, 741–751.
- NHS Management Executive (1992). *Assessing the Effects of Health Technologies*. Department of Health: London.
- Paykel, E. S. & Priest, R. G. (1992). Recognition and management of depression in general practice: consensus statement. *British Medical Journal* **305**, 1198–1202.
- Royal College of Psychiatrists (1993). Defeat depression. *Psychiatric Bulletin* **17**, 18.
- Shea, M. T., Elkin, I., Imber, S. D., Sotsky, S. M., Watkins, J. T., Collins, J. F., Pilkonis, P. A., Beckham, E., Glass, D. R., Dolan, R. T. & Parloff, M. B. (1992). Course of depressive symptoms over follow-up: findings from the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *Archives of General Psychiatry* **49**, 782–787.
- Stocking, B. (1992). Promoting change in health care. *Quality in Health Care* **1**, 56–60.
- Wing, J. K., Barbor, T., Brugha, T., Burke, J., Cooper, J. E., Giel, R., Jablensky, A., Regier, D. & Sartorius, N. (1990). SCAN: Schedules for Clinical Assessment in Neuropsychiatry. *Archives of General Psychiatry* **47**, 589–593.