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 (continuance 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 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 than 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

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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 NIH 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 under-treatment 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
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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.

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REFERENCES


