Optimising antidepressant use in clinical practice: 
towards criteria for antidepressant selection

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Background  Current treatment for depression in primary care and other 
out-patient settings demonstrates a pattern that is incongruous with the 
magnitude of the burden of depression suggested by its associated disability.

Aims  To review important considerations in current depression 
treatment with a focus on antidepressant use.

Method  Factors influencing the under-treatment of depression in real-world settings are examined.

Results  Patient and clinician behaviour as well as the incentives created by the health care system affect the likelihood of realising effective antidepressant therapy in practice.

Conclusions  Given the complexities of clinical practice, selection criteria for an antidepressant should include safety, efficacy and tolerability, as well as the ability of the antidepressant to deliver real-world efficacy while balancing health care costs in the long term.

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Being psychologically distressed, and of these patients, slightly more than half are 
prescribed antidepressant medication (Wells et al, 1989b; Simon et al, 1995).

When patients are treated for depression in primary care or another out-patient setting, 
they receive pharmaceuticals about 75% of the time. Clinical trials of antidepressants 
suggest an efficacy rate approaching 80% (Anderson & Tomenson, 1994). However, 
in terms of criteria for adequate dose and duration of treatment, only about 25% of 
patients in clinical practice are adequately treated when they are prescribed antidepressants 
(Katon et al, 1992; Lepine et al, 1997), even with the better-tolerated selective sero-
tonin reuptake inhibitors (SSRIs) (Dunn et al, 1998). Thus, the promise of effective treat-
ment implied by clinical trial efficacy rates for antidepressants is not realised in clinical 
practice owing to a variety of complex interactions between patient, provider and 
health-system characteristics. This situation in primary care and other out-patient clinic 
settings improved gradually over the 1990s but remains sub-optimal in most health care 
delivery systems.

ANTIDEPRESSANT THERAPY

The goals of antidepressant therapy of depression are well known: removal of 
symptoms, restoration of patient functioning and prevention of relapse or recur-
rent episodes. Consensus guidelines have been issued by the British Association for 
Psychopharmacology (1993) and the Royal College of Psychiatrists (1992) for the man-
agement of depression with antidepressants. These guidelines recommend that for treat-
ment to be effective, antidepressants should be prescribed at a dose shown by clinical 
trials to be effective in treating depression, and continued for at least 4 months beyond 
initial symptom resolution (with a longer duration for subsequent episodes). These 
guidelines are broadly consistent with other consensus groups’ recommendations 
(World Health Organization Mental Health Collaborating Centers, 1989; Agency for 
Health Care Policy Research, 1993). In addition to antidepressant therapy with 
adequate provider follow-up, accurate diagnosis, practical support and problem-solving 
techniques are important elements in primary care management of patients with depression.
The advent of better-tolerated antidepressants (beginning with the SSRIs and other new drugs) and the initiation of numerous educational programmes to increase the awareness of the burden of depression (Priest, 1994; Paykel et al., 1997) had the potential to improve antidepressant prescribing. Sadly, the evidence from clinical practice still shows that few patients receive an adequate dose or duration of antidepressant therapy (Donoghue & Tylee, 1996; Katzelnick et al., 1996; MacDonald, 1997; Rosholm et al., 1997; Donoghue, 1998; Dunn et al., 1998; Gregor et al., 1998). This suggests that while broadly based educational awareness policies and innovative drugs are necessary, they are not sufficient for improving antidepressant prescribing. Because many factors influence antidepressant prescribing, no single approach is likely to be sufficient to optimise depression treatment.

Many factors influence the effectiveness of antidepressant use in clinical practice, including the illness itself, pharmacological features of specific antidepressants (such as side-effects and dosing regimens) and individual behaviour (Demyttenaere, 1998). At a basic level, people with depression may not seek help for their mood disorder symptoms, focusing instead on somatic concerns such as gastrointestinal complaints, fatigue or headaches. Some people may refuse to pursue treatment because of the stigma attached to a mental diagnosis or because they believe they should be able to ‘handle it’ on their own. Another reason for under-diagnosis of depression by providers is the fear of alienating patients by suggesting that they have symptoms of depression. Finally, many general practitioners lack the time that is required to assess depression; when providers do identify the need for psychiatric evaluation, their patients may be reluctant to follow through on referrals.

Additional factors emerge once a patient is prescribed an antidepressant. These factors include inadequate dose and duration of therapy, as well as compliance issues. Indeed, taking medication in accordance with the prescription’s instructions is perhaps the single most important determinant in translating a drug’s efficacy demonstrated in controlled clinical trials into its effectiveness in clinical practice. Between 30% and 60% of patients do not take their medications as prescribed (Cramer, 1995; Demyttenaere, 1997). While reasons for this include pharmacological factors such as side-effects or adverse events, compliance is affected particularly by the beliefs and behaviour of both patients and prescribers. For example, patients may feel guilty about taking the medication, or even that they are underserving of it. They may sometimes believe they do not need the medication once they begin to feel better. Patients taking psychotropic medications such as antidepressants may worry that continuing the medication could result in a drug dependency (Priest et al., 1996) or a loss in its effectiveness (Donovan & Blake, 1992). The social stigma attached to mental disorders and associated pharmacological treatments may also inhibit patients’ intake of their medications (Fawcett, 1993). Prescribers can undermine compliance by advising ‘drug holidays’ to minimise side-effects such as sexual dysfunction, even though this practice is not recommended (Demyttenaere, 1997).

At the system level, a primary reason for sub-optimal treatment of depression is the lack of adequate health insurance coverage for long-term psychopharmacological management and other services by mental health professionals. The influence of health care financing arrangements has made it less attractive for providers from different specialities (for example a primary care physician and a psychiatrist) to collaborate, although such an approach shows promise for the treatment of depression (Katon et al., 1995). Managed care organisations or other insurance arrangements that exert control over which pharmaceuticals are listed in their formularies or are available to prescribers limit the availability of a wide range of antidepressant treatment options for providers and plan members. Finally, a narrow focus on controlling direct health care costs, even when the societal benefits of treatment are great, leads to the promotion of shorter-term interventions that do not address the chronic and recurrent nature of depression.

**Antidepressant Selection Criteria**

One approach to improve the selection of an antidepressant agent at the individual prescriber level may be for the prescriber to systematically consider five characteristics of the drug: efficacy, safety, tolerability, real-world efficacy and economic value. The first three characteristics are traditional criteria used in selecting an antidepressant. The latter two are important in light of how people actually behave and reflect growing concerns about costs.

**Conclusion**

Including the five criteria of efficacy, safety, tolerability, real-world efficacy and economic value, along with the individual patient’s current symptom profile and other medical history, in deciding which
antidepressant drug to select can help to realise in clinical practice the value of antidepressants as demonstrated in clinical trials, while at the same time balancing health care costs.

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