Bipolar disorder: new understandings, emerging treatments

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The role of general practitioners in managing bipolar disorder is gaining increasing recognition

ipolar disorder is attracting an upsurge of interest among the general public and in clinical and research arenas, which is being driven largely by the emergence of a range of new pharmacological and psychological treatments. It is also associated with an increasing awareness that bipolar disorder is more common than previously thought and often carries a significant burden of disability, which affects the patient, his or her family and society at large, particularly when the illness is not treated early and effectively. Indeed, using the disability-adjusted life-year (DALY) index (which represents lost years of healthy life), bipolar disorder is ranked at about the 80th percentile of disorders, only slightly below that for alcohol use and ahead of many physical illnesses. There is also increasing recognition of effective treatment modalities and, in particular, the role of general practitioners in the management of patients with bipolar disorder. Articles in this Supplement address a number of key areas with respect to recognising, monitoring and managing bipolar disorder in general practice.

An immediate area of controversy in clinical and research circles is how common bipolar disorder is. Australian data from the National Survey of Mental Health and Wellbeing indicate that there is a lifetime risk of bipolar disorder of 2.9%, being slightly higher in men (3.0%) and lower in women (2.7%); overall population prevalence is about 1.8%.2 However, as Tiller and Schweitzer (see page S5) discuss in this Supplement, prevalence estimates can be affected by how one defines the disorder, and whether one counts the "softer" forms of bipolar disorder which have been championed by some as being part of a broader bipolar spectrum. This is not an arcane debate, as the spectrum potentially includes a larger number of individuals than formal bipolar I disorder, and core management decisions hinge on correctly conceptualising whether the softer forms of bipolarity fall better within a unipolar or bipolar rubric. There is also debate about whether related illnesses such as borderline personality disorder fit into the bipolar spectrum.

Mitchell and colleagues (see *page S10*) take a pragmatic, probabilistic approach to diagnosing and monitoring bipolar disorder in general practice. Specifically, they emphasise useful clues to diagnosing bipolar depression; this has important therapeutic implications as the use of antidepressants without mood stabiliser cover can have detrimental effects in many patients with bipolar disorder.

Parker tackles the often neglected area of comorbidity in bipolar disorder (see *page S18*). He emphasises the high rates of anxiety disorders, obsessive compulsive disorder, and alcohol and illicit substance use disorder, and considers four models that might explain why such comorbidity is so common: bipolar disorder is associated with an increased rate of antecedent and *forme fruste* conditions; the bipolar condition increases the chance of the other condition; the other condition increases the chance of bipolar disorder emerging; and higher-order factors increase the chance of both the bipolar disorder and the other condition as interdependent or independent disorders (and so creating spurious comorbid-

ity). He applies each of these models to a consideration of how comorbidities can be managed in clinical practice.

An area of comorbidity worthy of mention is that of medical problems. It is well recognised that people with severe mental illnesses carry a high burden with respect to physical health problems, especially those associated with increased risk of cardio-vascular disease. Some of the medications used to treat bipolar disorder — notably, some of the atypical antipsychotics and mood stabilisers such as sodium valproate and lithium — can also contribute to this burden. The GP has a critical role to play in preventing (where possible), assessing, monitoring and treating such comorbidities, while psychiatrists also have a critical role in ensuring that this happens. Education of patients and shared decision making with patients are also important to ensure that patients understand the need for (and can request) metabolic and other screening tests.

Risks associated with bipolar disorder include the risk of suicide, specifically in the depressed pole of the illness. Suicidal assessments which focus on how the person is feeling as well as his or her experience of symptoms are of utmost import. But there are numerous other risks, including overspending and damage to reputation in the elevated pole, which are distressing and often embarrassing. Bassett (see *page S21*) provides an overview of these risks, and suggests ways the GP might work with the patient, the patient's family and other service providers to monitor and deal with risks and their consequences.

Three articles in this Supplement concentrate on treatment. Malhi and colleagues (see page S24) review recent guidelines for the pharmacological treatment of bipolar disorder, considering acute manic and depressive phases, and then turning to maintenance pharmacotherapy. Lauder and colleagues (see page S31) complement this by a consideration of the expanding literature on psychosocial treatments for bipolar disorder, and suggest elements of these that can be used by GPs in clinical practice. Berk and colleagues (see page S36) explain that bipolar disorder is associated with an active process of neuroprogression. Oxidative, inflammatory and neurotrophic factors play a role in the process, and both available treatments and novel options affect these pathways. Finally, Piterman and colleagues (see page S14) consider how best the GP can understand and work effectively with mental health services in delivering the best and most comprehensive care for their patients with bipolar disorder.

Although the articles in this Supplement have rightly focused on the distress and disability often experienced by people living with bipolar disorder and the need for optimal treatments, we must also remember that many people live full, productive and fulfilling lives while managing their condition effectively. In this regard, there is a significant bias in the literature, in that patients who have been ill and have recovered are rarely recruited for clinical trials. Studies are generally composed of the most unwell patients who attend tertiary settings, where the research is concentrated, and this is then generalised to the general population. The resultant data tend to be subject to significant sampling

bias, predominantly towards higher severity of illness and more adverse outcomes.

The welcome advances in research and treatments for bipolar disorder must be complemented by comprehensive and sustained activity to improve community awareness of early signs and symptoms, encourage appropriate help-seeking behaviour, and foster understanding and supportive community and health worker attitudes. Otherwise, early identification and treatment of bipolar disorder (and other mental illnesses) will remain wishful thinking. State and federal government commitment to such a campaign through the Fourth National Mental Health Plan, recently endorsed by the Australian Health Ministers' Advisory Council, is welcome, and progress will be monitored with great interest. The role of governments, clinicians and workers in community recovery and rehabilitation programs is to enable effective and early treatment to happen more often, for more people, and earlier in the course of illness.

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References

- 1 Access Economics. Bipolar disorder: costs. An analysis of the burden of bipolar disorder and related suicide in Australia. Melbourne: SANE Australia, 2003.
- 2 Australian Bureau of Statistics. National Survey of Mental Health and Wellbeing: summary of results. Canberra: ABS, 2007. (ABS Cat. No. 4326.0.)

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