# Recent advances in the management of depression and psychopharmacology

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**Objective.** To review the recent advances in the management of depression and psychopharmacology. **Data sources.** *Medline* and non-*Medline* literature search.

**Study selection.** The following key words were used: depression/therapy, depressive disorders, antidepressant, psychopharmacology, and mental health services. Years of study: 1988 to 1998.

**Data synthesis.** Recent advances in research on depression have confirmed that it is a common, recurrent, and disabling medical disorder. The latest epidemiological studies from the United States suggest that its lifetime prevalence is more than 17%, while a lower, but still substantial, proportion of Chinese people have the same disorder. The highly recurrent nature and conspicuous morbidity of depression call for the continuation of antidepressant treatment beyond the initial resolution of symptoms. For the first episode of depression, 6 to 9 months of adequate antidepressant treatment is indicated. For patients with recurrent depression, maintenance therapy for several years is needed. The increasingly widespread use of selective serotonin re-uptake inhibitors and other newer antidepressants has increased the direct drug cost, but the total health care expenditure may not be raised and may even be reduced.

**Conclusions.** Proper recognition and management of depression at both the clinical and health care policy levels are urgently needed.

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Key words: Antidepressive agents; Depression/therapy; Depressive disorder; Health policy; Mental health services; Recurrence

## Introduction

Non-psychotic mental disorders are considerably more common than psychotic disorders and they carry conspicuous morbidity and mortality. Popular misconception towards mental disorders and the prevailing stigmatising attitude among both the general public and professional staff remain major barriers to the treatment and recovery of mentally ill patients. Over the past few decades, the advancement of psychiatric research has provided a better understanding of the prevalence, aetiology, treatment, and outcome of various mental disorders, especially depression. In addition, the availability of newer, safer, and better-tolerated drugs has improved the treatment of mental

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illness. The introduction of selective serotonin re-uptake inhibitors (SSRIs) as new antidepressants indicates that the development of psychotropic drugs has shifted from serendipitous discovery to rational and theory-based design. Not only has psychiatric research helped improve our understanding of the underlying mechanisms and thus conceptualisation of mental disorders, it has also brought about refinement in prescription practice. These advancements and their cost implications in Hong Kong are discussed in this paper.

#### **Depression is very common**

Although unhappiness is usually a normal human experience, it differs from clinical depression in both duration and severity. Depression should be recognised as a clinical syndrome that is characterised by a cluster of emotional, behavioural, and cognitive features. The important conceptual shift in viewing depression from a problem of human weakness to a medical

and usually chronic recurrent disorder similar to that of hypertension and diabetes mellitus has paved an important step for the proper recognition and treatment of depression.

Different classification systems of depression exist and have changed over the years. The two most wellaccepted international systems are the Diagnostic and Statistical Manual (DSM-IV) of the American Psychiatric Association<sup>1</sup> and the International Classification of Disease and Related Health Problems (ICD-10) of the World Health Organization (WHO).<sup>2</sup> Both are systems that have well-defined operational criteria. Depression is mainly classified into major depression and dysthymia. An individual with major depression has a persistent low mood; anhedonia; negative cognition; and disturbances in sleep, appetite, and general activity for more than 2 weeks (Box). If the individual has only depression without mania, the diagnosis is unipolar depression. If manic or hypomanic episodes are present, the diagnosis is bipolar affective disorder. Major depression can be mild, moderate, or severe in intensity. Dysthymia is a low-grade persistent depression that has lasted for 2 years or longer. Adjustment disorder describes a person's transient unhappiness in facing loss or other stresses and is expected to recover once the stress is over or adapted to.

Depression has a high prevalence across all ethnic groups, socio-economic class, and locality. The Epidemiology Catchment Area Study, which was performed

#### Common features of depression

#### Core symptoms

- (1) Low mood
- (2) Loss of interest (anhedonia)
- (3) Fatigue or reduced energy

#### Additional features

- Negative cognition (excessive guilt, hopelessness, and worthlessness)
- (2) Suicidal ideation
- (3) Disturbed sleep
- (4) Change in appetite and weight
- (5) Inattention and poor memory
- (6) Psychomotor retardation or agitation

#### Diagnostic features

- (1) Persistent symptoms for more than 2 weeks
- (2) ICD\*-10 classification requires two of the three core symptoms plus additional symptoms
- (3) DSM†-IV classification requires either low mood or anhedonia plus additional symptoms
- (4) Atypical symptoms like hypersomnia, increased appetite, weight gain also present in a proportion of depressed patients
- (5) Anxiety symptoms are also commonly present in depression
- \* ICD International Classification of Diseases

in the United States in early 1980s, found that depression has a lifetime prevalence that ranges from 2.3% to 4.4% and 4.9% to 8.7% for male and female Caucasian populations, respectively.3 The more recent and the first nationally based National Comorbidity Study, also performed in the United States, revealed an even higher lifetime prevalence of 17.1% (12.7% for men and 21.3% for women); the current 12-month prevalence is 10.3% (7.7% for men and 12.9% for women).<sup>4</sup> The increase in the preponderance of women with depression has been a consistent finding and has been confirmed by a recent WHO collaborative study of psychological problems in general health care in 15 medical centres across four continents.<sup>5</sup> Epidemiological data for Chinese patients with depression are more limited. Using a similar diagnostic instrument to that used in the Epidemiological Catchment Area Study, two separate research groups—one in Hong Kong<sup>6</sup> and one in Taiwan<sup>7</sup>—found that Chinese male and female subjects had a lower lifetime prevalence of depression (1.29% and 2.44% for men and women in Hong Kong, respectively, and 0.9% and 1.7% for men and women in Taiwan, respectively). Both studies, however, were conducted in the early 1980s and based on fully structured interviews by non-clinical research staff. There is a dearth of data concerning this intriguing discrepancy between the Chinese and Caucasian populations. The apparent lower prevalence of depression in the Chinese population may be related to a lower prevalence of alcohol use, a better social and family support system, more anxiety presentation instead of depression, and also perhaps an underreporting of depression by the general public in relation to their fear of stigmatisation.6 The exact reason is still unclear. In contrast, studies of Chinese communities in the United States have usually indicated a higher prevalence of depression.<sup>3,4</sup> It is likely that methodological and social factors may have played a role in the underestimation of the true prevalence of depressive disorders in Hong Kong, Taiwan, and mainland China. Nevertheless, many Hong Kong people do suffer from depression at some point in their lives, and reports have shown that depression is becoming more common in younger people. 8 Clinically, depression is even more common among hospitalised and chronically ill patients. Numerous studies have reported an increased prevalence of 30% to 50% among patients who have a malignant tumour, myocardial infarction, or stroke.9

#### **Depression is serious**

Depression is associated with a serious impairment of social, marital, and occupational functioning, as well

<sup>†</sup> DSM Diagnostic and Statistical Manual

as prominent personal and interpersonal distress.<sup>10</sup> In 1993, the World Bank estimated that depression constituted 17% of disability associated with mental health problems worldwide.<sup>11</sup> Furthermore, depression is currently the fourth most common disabling disease in the world and it has been predicted that it will be the second most common, after ischaemic heart disease, by the year 2020.<sup>12</sup> Depression also poses a significant economic burden to society, as it will lead to reduced productivity, treatment cost, and loss of human life by suicide.<sup>13</sup> More than half of the economic burden will be accounted for by reduced productivity.<sup>13</sup> The current cost due to depression has been estimated to be similar to that of cancer and ischaemic heart diseases.<sup>14</sup>

# The long-term course of depression

Recent studies of the long-term outcome of depressive illness reveal that the disorder is a chronic and highly recurrent one. The improvements suggested by the Pittsburgh group regarding the delineation of the different phases of the course of depression and the distinction between symptom re-emergence and episode recurrence have been well received by psychiatric professionals.<sup>15</sup> The acute phase of treatment after the onset of depressive symptoms aims to stabilise the symptoms. The continuation phase will continue to stabilise the patient for a further 3 to 6 months. If the depressive symptoms return during this period, the patient is considered to have had a relapse of the same depressive episode. The maintenance phase aims to prevent the future recurrence of a new depressive episode. 15 Long-term follow-up studies of patients treated in psychiatric facilities have shown that 20% to 25% of those who had recovered from the first episode of depression had a recurrence within 1 year, 30% of patients had become chronically depressed, and only less than 25% remained well for 10 years or longer. 16,17 In other words, the chance of having a second episode after the first one is 50%, and the chance of a third episode occurring will increase to between 80% and 90%. This kindling-like phenomenon is also commonly encountered in other recurrent medical disorders such as epilepsy, and requires early and long-term intervention. In addition, 10% to 15% of patients with depression, especially if they are hospitalised commit suicide by 10 years.<sup>18</sup>

Despite its prominent clinical, psychosocial, and economic burdens, depression has been underrecognised and undertreated. Only a small proportion of depressed subjects (<10%) receive appropriate treatment or drug treatment of a sufficient dosage and

duration.<sup>19,20</sup> Reasons may include inadequate access to care, underdiagnosis, undertreatment, poor patient compliance, fear of stigmatisation, and preference for alternative psychosocial therapy.

# Recent understanding of the aetiology of depression

Although mental disorders are common and involve signs and symptoms that cluster recognisably as syndromes, the aetiology of the majority of mental disorders is multifactorial. Depression is no exception. In fact, depression offers a good model to understand the complexity and multiple interactions among biological, psychological, sociocultural, and political domains that ultimately culminate in mental disturbance. In particular, depression is often predisposed by genetic influences, developmental problems such as low self-esteem, chronic sociopsychological adversity, and lack of a social and family support network. Frequently, the onset of depression is preceded by significant life events.21 There follows a chain of neurobiological changes, which include disturbed sleep, hormonal changes, the reduced release of neurotransmitters (particularly monoamines), and altered gene expression. A clinical syndrome of depression with mood, cognitive, somatic, and behavioural changes thus results.22

#### **Treatment of depression**

The established modes of treatment of depression consist of antidepressants, electroconvulsive therapy, formal psychotherapy, and—depending on the availability of resources and factors pertaining to helpseeking—a combination of these treatments. Less common methods include bright-light therapy for seasonal affective disorder, or sleep deprivation for resistant cases of depression. Of all the available methods, the mainstay treatment is antidepressant therapy. While electroconvulsive therapy is a very effective treatment, it is usually reserved for patients with severe depression who refuse food or who are actively suicidal and hence require rapid treatment. Social and family support is very important in predicting the outcome and recovery of depressive patients. The most established psychotherapies that are thought to be useful in treating depressed patients are cognitive and interpersonal psychotherapy. Although the role of psychotherapy alone in the management of recurrent depression seems to be less promising than antidepressants alone,<sup>23</sup> its role as adjunct therapy to medication treatment in dealing with marital, familial, social, and occupational problems that often

Table 1. Classification of antidepressants

Conventional (first-generation)	New (second- generation)	Newest
TCAs* Tertiary amines imipramine amitriptyline Secondary amines nortriptyline  MAOIs† Phenelzine	SSRIs <sup>‡</sup> Fluoxetine Fluvoxmaine Paroxetine Citalopram Sertraline  RIMA <sup>§</sup> Moclobemide	Newer SSRIs Nefazodone NaSSAs <sup>I</sup> Mitrazapine SNRIs <sup>II</sup> Venlafaxine
	Newer TCAs Dothiepin Doxepin Lofepramine	
	Heterocyclics Bicyclics trazodone Tetracyclics mianserin	

\* TCAs tricyclic antidepressants

† MAOIs monoamine oxidase inhibitors

† SSRIs selective serotonin re-uptake inhibitors

† RIMA reversible inhibitors of monoamine oxidase A noradrenergic and specific serotonergic antidepressants

accompany long-standing depression is established.<sup>24</sup> Because of the severe shortage of mental health professionals, however, the treatment of depression is largely pharmacological in Asian countries, including Hong Kong.

selective noradrenergic serotonin re-uptake inhibitors

# Advances in antidepressant treatment

#### Classes of antidepressants

¶ SNRIs

The original discovery of antidepressants was serendipitous and took place about four decades ago. The two main traditional types of antidepressants were tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). In the past two decades, the biological treatment of depression has improved with the availability of newer, safer, and better-tolerated antidepressants. The various classes of antidepressants currently available are shown in Table 1.

The main conventional group of antidepressants consists of TCAs such as amitriptyline and imipramine. The neurotransmitter actions of the TCAs include not only the blockade of the re-uptake of noradrenaline (NA) and serotonin (5-hydroxytryptamine [5HT]), but also prominent anticholinergic, antihistaminergic, and anti-adrenergic effects.<sup>25</sup> While the enhancement of the effects of both NA and 5HT is thought to be therapeutic, the blockade of other neurotransmitter systems results in prominent side effects, especially

Table 2. Side effects of tricyclic antidepressants and selective serotonin re-uptake inhibitors

TCAs*	SSRIs <sup>†</sup>
Dry mouth Blurred vision Sedation Weight gain Postural hypotension and fall Cardiac arrhythmia Constipation Cognitive impairments	Nausea Headache Sleep disturbances Sexual dysfunction Anxiety Apathy

<sup>\*</sup> TCAs tricyclic antidepressants

anticholinergic, cardiac, and neurological ones (Table 2). Subsequently, there may be drying of the mouth, blurred vision, constipation, sedation, and postural hypotension. Cognitive impairment may also occur and this may be dose- and age-related.<sup>26</sup> The most dangerous problem associated with using TCAs, however, is their propensity to cause death when they are taken as an overdose in a suicidal act.<sup>27</sup> Such an event act could result in grave medico-legal consequences for the prescribers.

The irreversible MAOIs such as phenelzine (which is the only MAOI available locally) make up the other group of conventional antidepressants. Patients need to take a rather strict MAOI regimen and need to be very cautious about any potential drug interaction to avoid precipitating hypertensive crisis. The foods that need to be avoided include any fermented product such as cheese, fermented bean curd, and soy sauce. It is generally safe for patients taking MAOIs to eat food containing monosodium glutamate.<sup>28</sup> Consequently, the use of conventional MAOIs has been limited by food and drug restrictions, although MAOIs are still occasionally used to treat resistant cases of depression. Second-generation antidepressants include newer TCAs such as dothiepin, doxepin, and lofepramine; and heterocyclic compounds such as trazodone and mianserin. Each of these cyclic compounds, however, has side effects.

Over the past decade, the availability of SSRIs has markedly influenced the prescription pattern of antidepressants. This newer group of drugs consists of chemically diversified compounds that selectively inhibit serotonin re-uptake, while having minimal action on other neurotransmitter systems. There are five SSRIs available locally: fluoxetine, fluvoxamine, paroxetine, citalopram, and sertraline. They are similar in efficacy and differ mostly in terms of pharmacokinetic differences, potential drug interactions due to cytochrome P450 enzyme inhibition, and side effects.<sup>29</sup> Side effects of SSRIs occur less commonly than those

<sup>†</sup> SSRIs selective serotonin re-uptake inhibitors

of TCAs and include nausea, headache, sexual dysfunction, and sleep disturbances (Table 2). Sometimes, taking SSRIs may also lead to apathy, lethargy, and extrapyramidal side effects. These effects are thought to be mediated through the inhibitory action of serotonin on dopaminergic neurons. A potentially fatal serotonin syndrome, which is characterised by confusion, disorientation, autonomic hyperactivity, and neuromuscular features (such as clonus and ataxia), has been reported rarely and is associated especially with combination therapy with other serotonergic compounds such as MAOIs. A

Another new group of antidepressant consists of the reversible MAOIs, which are also known as reversible inhibitors of monoamine oxidase A (RIMA). Moclobemide is the typical example. The advantage of RIMA over conventional MAOIs is the greatly reduced potential for food and drug interactions. Like the SSRIs, they are generally safe in overdoses and do not cause undue sedation.

#### Subtypes of serotonin receptors

In parallel with the development of new antidepressants, there has been a rapid advancement of neuroscience and a greatly enhanced understanding of the various subtypes of 5HT and NA receptors. Seven major subtypes of serotonin receptor have been cloned so far. They differ in terms of pharmacological property, signal transduction mechanism, and gene sequence.<sup>30</sup> The 5HT<sub>1a</sub> receptor is both a somatic autoceptor that controls the firing rate of 5HT neurons and a postsynaptic receptor. It thus closely governs mood regulation. The 5HT<sub>1b/d</sub> receptor is a terminal autoceptor, which controls the release of 5HT; however, its exact role in depression is still unclear.<sup>31</sup> The 5HT<sub>2a-c</sub> receptor has been implicated in sleep, sex, and appetite regulation, whereas the 5HT<sub>3</sub> receptor is involved in the gratification response and drug abuse. The functions of other subtypes of receptors in psychiatric-related disorders remain to be investigated.

The newest group of antidepressants (Table 1) is designed to target specific biological systems. Nefazodone is structurally related to trazodone and is sometimes described as a second-generation SSRI; it exerts a modest inhibition of 5HT re-uptake and blocks  $5HT_2$  subtype receptors. Nefazodone has been reported to cause a lesser extent of side effects such as sleep disturbance and sexual dysfunction. Mitrazapine is a noradrenergic and specific serotonergic antidepressant (NaSSA) and blocks the  $\alpha_2$  autoceptor and heteroceptor; it thus enhances the release of both 5HT and NA, while blocking  $5HT_2$  and  $5HT_3$ 

receptors.<sup>33</sup> As a result, mitrazepine has anxiolytic and sleep-improving properties.<sup>33</sup> Venlafaxine is a dual-action antidepressant that enhances both NA and 5HT systems (a selective noradrenergic-serotonergic re-uptake inhibitor [SNRI]), but is devoid of any anticholinergic effect.<sup>34</sup> The involvement of the dopamine system in depression has also led to the use of bupropion in treating depression, especially in combination with other antidepressants.

#### Comparision of old and new antidepressants

The main advantage of new antidepressants is their safety during an overdosage. Increasingly, new antidepressants are being prescribed instead of the conventional TCAs as the first-line treatment in newly diagnosed cases of depression. A justification for this practice is the worry of medico-legal consequences of prescribing TCAs when safer alternative drugs are available. 35,36

Randomised controlled trials and meta-analyses of various studies have confirmed that the new antidepressants have a similar efficacy to TCAs. Controversies exist, however, as to whether the new antidepressants, particularly SSRIs, will have a lower discontinuation rate than TCAs. An earlier metaanalysis by Song et al<sup>37</sup> did not demonstrate any superior effects of SSRIs over traditional TCAs. A subsequent meta-analysis that had better inclusion criteria suggested that the discontinuation rate was 10% lower for SSRIs than for TCAs; the drop-out rate was also 25% less in the SSRI group.<sup>38</sup> Recently, it has been shown that although SSRIs have a lower discontinuation rate than older-generation TCAs, the discontinuation rates do not differ significantly from the newer-generation tricyclic and heterocyclic antidepressants.39

Whether SSRIs can work as effectively as TCAs in treating severe depression is also controversial. In a recent meta-analysis comparing 25 studies of SSRIs and TCAs that were used to treat depressed in-patients, the dual-action TCAs were found to have superior efficacy but were more poorly tolerated than SSRIs.<sup>40</sup> The TCAs may be a better choice in severe depression, although the high risk of suicide by overdose among the severely depressed should be borne in mind. Further studies are needed to investigate whether the new antidepressants work better for severe or treatment-resistant cases.

#### Future development of antidepressants

The currently available new antidepressants are safer and better tolerated. Among compliant patients, however, new antidepressants do not seem to be more effective than conventional drugs. Both classes of drug are also limited by the delayed onset of their therapeutic action of about 2 weeks. Accordingly, future drug development should aim at producing antidepressants that work faster. Preliminary evidence suggests that targeting subtype receptors—for example, by using a combination of a blocker of the 5HT<sub>10</sub> autoceptor such as pindolol, and an SSRI—may accelerate the antidepressant response.<sup>41</sup> This effect is thought to occur through the blockade of the 5HT<sub>1a</sub> autoceptor that controls the firing rate of the 5HT neurons. Another line of drug development is to target signal transduction at the secondary messenger level. Until new antidepressants with novel mechanisms are available, the current emphasis on the monaminergic system will remain.

#### Duration of antidepressant treatment

The clinical course of depression is typically recurrent and chronic, and antidepressant therapy should be divided into three phases: the initial acute phase, the continuation phase, and the maintenance period that prevents further recurrence of depression.<sup>15</sup> The acute phase can usually be accomplished within 3 months. In the past, treatment was tapered off once symptom resolution was achieved. However, frequent relapses of symptoms and recurrences of depression usually followed. Accordingly, various national and international medical bodies, including the WHO and the American Psychiatric Association, have recommended that antidepressant therapy be continued for at least 3 to 6 months beyond symptom resolution. 42,43 Recent data have substantiated the effectiveness of continuation treatment with SSRIs.44,45 Maintenance therapy is also needed for recurrent depression. The duration of effective maintenance treatment depends on a number of factors, which include the age of onset, number of episodes, severity of episodes, family history, presence of double depression (major depression coexisting with dysthymia), and initial response to treatment.46 A seminal study performed in the United States showed that only 20% of cases of depression recurred during a maintenance regimen of imipramine, whereas 80% of cases in the placebo arm recurred.<sup>23</sup> For an initial episode of depression, 6 to 9 months of antidepressant treatment have been recommended, while for patients with more attacks of depressive episodes or who are at risk of recurrence, maintenance therapy for 4 to 5 years will be needed. For high-risk patients, even longer-term—and frequently lifelong maintenance—is indicated. The drug dosage for effective maintenance is recommended to be the same as the initial treatment.<sup>23</sup>

## **Implications for psychiatric services**

Even in the West, only a small proportion of patients with depression receives adequate duration of therapy at an adequate dosage<sup>17,47</sup>; the majority of cases are undiagnosed and untreated. The need for an increase in awareness of depression and its adequate treatment thus cannot be overemphasised. Locally, the attention to psychiatric illness and services has been even more inadequate. Mental disorder is mostly equated with schizophrenia and bipolar manic depressive psychosis, which have much lower prevalences than depression in the local community. The psychiatrist to population ratio in Hong Kong has been consistently low and is only one fifth to one seventh of that found in developed countries in which mental health issues are given more attention. It is time for Hong Kong to evaluate the manpower of psychiatric health professionals. In addition, because a large proportion of depressed patients visit primary health care physicians, steps are needed to improve the recognition and management of depression by these physicians. The common misconception among the public, as well as some health professionals and policy-makers, that mental illness is not treatable, and the powerful stigmatising attitudes towards mentally ill patients will require educational efforts to reverse. Effective public educational campaigns that have been held in the United States and the United Kingdom are examples that Hong Kong can follow.

#### Implications of the treatment cost of depression

With the increasing tight health care budgets and soaring health care expenditure worldwide, important consideration must be given to the economic evaluation of treatment for depression. While much research is still needed in this important aspect, studies have supported the role of antidepressants in restoring the functioning and work performance of patients10 and in reducing disabilities. 48 However, the choice of conventional versus newer antidepressants, notably SSRIs, with respect to economic consideration has not been fully settled. While the direct drug cost of SSRIs is higher than that of TCAs, the total health care expenditure for patients taking SSRIs is equal to or lower than that of patients taking TCAs.<sup>13</sup> The reasons are as follows: higher chances of complications related to TCA treatment, more frequent physicians' visits for the TCA group, other health care expenditure such as plasma-level monitoring, and higher drop-out rates in the TCA group.<sup>13</sup> However, in a recent review article, Hotopf et al have criticised the rather 'crude' modelling approaches and the overestimation of attrition rates of cost-effectiveness studies.<sup>49</sup> The authors concluded that there is no evidence to suggest that SSRIs are more cost-effective than TCAs and suggested that the final verdict can be drawn only after a well-conducted prospective cost-effectiveness study.<sup>49</sup> Similarly, a study by the Canadian Coordinating Office for Health Technology Assessment has suggested that SSRIs are more cost-effective than TCAs alone as first-line treatment.<sup>50</sup> However, SSRIs have been found to be less cost-effective than initial combination treatment with TCAs followed by SSRIs in the dropout group.<sup>50</sup>

In the United States, TCAs accounted for 24% of antidepressant sales in 1993 and this dropped to 3% in 1998. Meanwhile, the sale of SSRIs increased from 68% in 1993 to 78% in 1998, and other new antidepressants constituted 18% of sales in 1998. A similar trend is being observed in other countries such as the United Kingdom and Australia (S Lee, written communication, 1999). If these trends continue, TCAs may become outdated within the next 5 to 10 years. Yet, in Hong Kong, the meagre drug budgets allocated on the basis of older-generation psychiatric drugs in public hospitals have greatly limited the use of the newer antidepressants, even when they are indicated. In one of the regional hospitals, the drug budget was overspent by nearly 200%, despite the limited acquisition of new antidepressant drugs (CM Leung, written communication, 1999).

The demand for antidepressant therapy with newer, safer, and better-tolerated antidepressant drugs will continue to grow. There is, of course, still a role for conventional TCAs, especially in severe cases of depression. Nevertheless, the medico-legal risk of initiating TCA therapy in depressive patients who are suicidal, and rising consumers' rights will shape the local pattern of antidepressant drug usage. In Hong Kong, there is a pressing need to evaluate the costeffectiveness of new drugs, compared with the conventional antidepressants, based on the concept of the total rather than direct cost of health care. Unless the governmental and relevant medical bodies recognise the huge public health burden of mental disordersdepression in particular—a crisis in the psychiatric service will continue to loom ahead.

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