

# Managing Depression as a Long Term Condition

## Introduction

Depression is a ubiquitous term which is used to denote a wide variety of mental conditions. In common language people use the term depression to refer to an experience of undesirable or negative emotions. However, in mental health practice, the term depression is used to refer to a specific syndrome characterized by a cluster of phenomena [1]. It is important to make this distinction as there has been valid concerns about the increase in antidepressant prescribing [2], which may be related to over diagnosis of depression [3]. The syndrome of depression is associated with changes in mood, biological functions, cognitive dysfunctions, and loss of pleasure [1]. All health care practitioners should be aware that such a syndrome and its variants can assume a chronic course. Therefore, strategies and very importantly-services to manage the condition with a chronic perspective are important.

Amongst the lay public chronic is often assumed to be irremediable, therefore use of the phrase long term condition may be more acceptable. It is important to consider that health education may be necessary to portray a long term approach as feasible and effective in the public's mind.

## Chronicity and Depression

The national co-morbidity study replication showed that the 12 month prevalence of major depression is 6.7% and about one third of these are in the severe category [4]. Severity of depression is an important predictor of chronicity [5,6]. Major depression is a remittent and recurrent condition with 80% chance of recurrence and an average of four life-time episodes [7]. Yet other estimates report 50% chance of recurrence after the first episode and 80% probability of recurrence after the second episode [8]. Recurrence by itself may does not imply long term treatment (for example certain types of migraine do not need ongoing treatment), but recurrence in depression is associated with cycle acceleration and increase in severity [9]. Antidepressant treatment reduces relapse rates in depression [10]. The number needed to treat to prevent a relapse with second generation antidepressants is 5 [11], with close to 70% reduction in relapse risk over 12 months of continuation antidepressant treatment [12].

Both biological and psychological evidence shows that recurrent depression is associated with enduring changes. Right hippocampal volume reduction has been associated with recurrence of depression [13]. Subtle neurocognitive deficits, seen in euthymic patients' with major depression [14-16]. Even in the absence of depressive mood, patients may have reduced emotional reactivity to positive and negative affect [17] and increased cognitive reactivity [18]. Subsyndromal and minor depression symptoms were the most common mood state in a longitudinal study of patients with unipolar depression [19], yet again highlighting the persistent nature of the disturbance.



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All of the above facets of depression are arguments for a longitudinal affliction rather than a phenomenon of isolated acute episodes.

## Association of Depression with Chronic Disease

9% to 23% of chronic disease sufferers have depression and association of depression with a physical disease leads to highest illness burden [20] as shown by data from 60 countries. Depression is also associated with an increased number of symptoms in chronic diseases [21]. Patients are less likely to comply with medical treatments in presence of depression [22]. Depression has a bidirectional relationship with chronic illness and can increase the cost of care of medical illnesses [23].

Depression and type 2 diabetes have a well-known reciprocal relationship [24]. Glycaemic control is impaired in the presence of depression in type 1 and type 2 diabetes [25]. Obesity increases the odds of depression and vice versa; being overweight increases the risk of depression [26]. Metabolic syndrome, a precursor of diabetes, can precede or follow depression [27]. Smoking is not only associated condition but is also linked with depression in adolescents [28]. Not surprisingly mental health improves with smoking cessation [29]. The risks for a range of cardiovascular illnesses increase with depression. It not only increases the risk of cardiac mortality post myocardial infarction (MI), but it also increases all-cause mortality post MI, after adjusting for cardiac disease severity [31]. This association has not changed over 25 years [32]. Presence of depression in chronic obstructive pulmonary disease is strongly associated with mortality [33] and affects the outcome of pulmonary rehabilitation [34].

The association of inflammation in depression may explain at least some of its links with chronic illnesses [35]. A recent meta-analysis showed a beneficial effect of celecoxib, a non steroidal anti-inflammatory drug, on depression [36].

This association of depression with long term conditions adds to the burden of illness and indicates that depression is not just a mental

illness but a complex phenomenon which affects physical and mental health.

### Disability is a Part of Depression

Depression is a disabling condition. Data from the World Health Organization shows that it is one of the most disabling health condition particularly in Europe & Americas [37]. A recent systematic review shows depression as the second most important cause of disability [38]. This review also showed that depression contributes to mortality in physical health conditions like ischemic heart disease.

Only 5% of clinical trials report functional outcomes in depression [39] since there is no regulatory requirement to report functional improvements. Therefore treatments for depression have not focused on disability. Functions appears to recover with symptom improvement in depression [40] but in a 3 year follow up there were persistent deficits in social and physical functioning [41]. Depression, its sequelae or inadequate treatment for both may contribute to disability which may be chronic or intermittent. There is an overall long term impact of depression beyond the episode of depression.

### The Play of Heritability and Environmental Factors in Depression

At 50 to 70% heritability, depression is a highly heritable illness [42] with estimates similar or more than chronic conditions like type 2 diabetes, cholesterol levels [41] and hypertension [43]. Whilst this is not an evidence for chronicity, it does indicate an enduring underlying predilection similar to other long term conditions.

So what might be the role of environmental factors in predicting the outcome of depression? Given that many chronic conditions with similar heritability have onset or outcomes affected by sociodemographics and life style factors, something similar could be expected of depression. This indeed appears to be the case. Similar to other chronic conditions the prognosis of depression is affected by adversity [44] and influences the treatment response [45]. Childhood adversity in particular has been linked with chronicity in depression [46]. This opens avenues for nonclinical interventions, which could reduce risk factors for development of depression. Such interventions do not have to be psychological or biological but may rest on improving sociodemographic conditions. A systematic review of befriending showed reduction in depressive symptoms and stress [47] in the community. At least one randomized controlled trial showed the beneficial effect of befriending in chronic depression in women [48] but more studies are needed to validate these findings.

### Do Current Treatments Consider Long Term Depression Management?

The arguments marshalled so far indicate an enduring diathesis and potential chronicity in the course of depression. If such be the case do the treatment approaches and service delivery match the long term nature of depression?

Many national recommendations suggest acute, continuation and maintenance phases of antidepressant treatment [49,50]. As mentioned earlier, long term treatment with antidepressants is worthwhile for improving treatment outcomes in depression. Amongst evidence based psychological treatments for depression

cognitive behavioural therapy (CBT), behavioural activation therapy (BAT) and interpersonal therapy (IPT) have been devised as acute treatments of depression [51-53]. At least two studies have shown equivalence of BAT to antidepressant treatment [54,55].

The relapse prevention effect of psychological treatment particularly CBT, can be realized through acute and continuation phase interventions [56]. A one year follow up of patients in acute treatment randomized controlled trial of BAT, cognitive therapy and antidepressant treatment showed that the psychological therapies were equivalent to antidepressants in preventing relapse [57]. There is some evidence that IPT treatment also has a relapse prevention effect in depression particularly in combination with antidepressant treatment [52]. Mindfulness based cognitive therapy (MBCT) is yet another modality for preventing relapse which is delivered in the remittent phase of depression and has been found to be effective [59]. An 18 month follow up study of MBCT showed equivalent effectiveness to antidepressants in relapse prevention [60]. Interestingly both cognitive and mindfulness approaches seem to be effective for relapse prevention for those patients who have experienced more than 3 episodes of depression [58]. However, there remain several unanswered questions: How long does the relapse prevention effect of acute psychological treatment last? What is the value of inter episode psychological treatment in preventing relapse? Can the effect of psychological treatment be prolonged through regular booster sessions over a number of years? Does psychological treatment also improve long term functional outcomes? Even if psychological treatment turns out to be as effective as medication treatment, the real challenge is to train therapists both in right quality and quantity to supply these treatments effectively.

Pharmacotherapy has convergent evidence on chronic treatment for depression and psychological therapies have emerging evidence in this area. Depression education has undue emphasis is on acute treatment rather than maintenance, relapse prevention and long term treatment [61,62]. Thus, the depressed client may not have expectation of a long term treatment strategy. Compare this to chronic conditions like diabetes where adherence education is integral to the treatment approach. Perhaps this partly explains why the antidepressant discontinuation rates in depression are very high at 50% [63] and surpass the figures for treatment non adherence in other common chronic conditions like diabetes and hypertension [64].

### Do current Service Provision Systems Reflect Long Term Management of Depression?

Since the literature guiding depression treatment has clearly justified long term treatment, is this reflected in practice and health care systems?

Study of diabetes revolutionized the management of chronic conditions and created the chronic care approach [65]. The central premise of this approach is to create a patient centred connected health care approach which provides a continuum of care to sufferers of these conditions. This is managed through networks of care which could be collaborative and matched to suit the clinical intensity of the condition. Table 1 summarises the components of this system.

Self-care is an integral component and effective component

**Table 1:** The Chronic Conditions Model [17].

Components
The Health System
Delivery System Design
Decision Support
Clinical Information System
Self-Management Support
Community Resources & Policies

of chronic conditions management [66]. At the clinical level good information systems are needed for operational effectiveness and decision supports systems are needed to embed evidence in practice [67]. Stepped care and collaborative in depression has borrowed heavily from this approach. Collaborative care -as defined by the use of nonmedical specialists to enhance depression management in primary care- has meta-analytic level evidence for short term and long term (up to 5 years) outcomes in depression [68]. A meta-regression analysis of collaborative care in depression showed that the ingredients determining effectiveness were: case managers with mental health background and specialist supervision [69]. Disease management programmes [70] based on principles of chronic care model also showed significant benefit in depression. Such an approach improves treatment adherence, long term outcome, patient and professional’s satisfaction [71]. It does increase the cost of medical care which is more than compensated by decrease in societal and disability costs. However such services are not routinely available. The improving access to psychological therapies (IAPT) is probably the largest service based stepped care intervention for common mental health disorders and the initial findings are promising [71]. However this service is focused on acute phase treatment with stepped psychological interventions.

Routine services in mental health do not provide provision do management based consistent with the chronic care model even though such an approach has robust evidence. Whereas in physical health problem like diabetes there is an implicit step down approach from specialist clinic to care in the community, all the stepped care pathways in depressions are really ‘step up’ approaches to treatment. Post recovery from acute episode routine follow up or discharge may ensue. Active monitoring of depression resurgence with early response system is conspicuously absent in routine services providing treatment for depression. Self-care post recovery is not clearly conceptualized as compared to chronic disease management in physical health.

### Vexing Problems and Potential Solutions

#### Public health education issues

Depression and ensuing disability is a problem of significant magnitude and public health education must be crafted to capture the long term perspective of managing depression. Current health education works towards stigma reduction, early detection, acute treatment and recovery. These are all valuable goals. A strong focus on long term management which covers maintenance, relapse prevention, symptoms monitoring and ways to access relevant clinical services is crucial. Reduction of risk factors and encouragement of

protective factors require further thought. For example exercise may be highlighted as a protective and therapeutic factor influencing mood [72,73].

#### Diagnostic and early detection issues

Diabetes can be diagnosed entirely based on simple repeatable laboratory investigations. This is not the case for depression. Diagnostic interviews are the gold standards but the reliability of gold standard interview also fluctuates considerably [74]. This is of serious concern, more so because these results are based on rigorous structured interviews whereas routine clinical encounters may have even less stringent standards.

One of the most commonly used scales in primary care PHQ-9, which is highly sensitive for detection of depression [75] has been called the ‘lab test’ for depression. However, PHQ-9 may not have a high positive predictive value for a current episode of major depression [76]. Screening for depression is not routinely recommended [77] due to high false positive rates and as it does not appear to change outcomes [78]. This can be partially explained by the fact that if services to manage depression are not available screening does not make a difference and if they are available screening is no longer necessary.

There are no simple answers to these issues. One potential solution could be to target recurrent depression with vigour. If recurrence be considered, it probably will increase diagnostic specificity and identify depression which is suitable for long term management.

#### Treatment issues

The availability of antidepressant medications is not an issue, as a large number of generics exist in the market in most economies. An inadequate treatment and antidepressant discontinuation rate is a problem in recurrent depression. However this may not be the only problem with pharmacological (or for that matter psychological) treatments. The Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) trial showed that treatment non response is fairly high in depression with remission rates of just around 50% after two sequential treatment steps and with remission rates of less than 25% in the third and fourth step [79]. This is hardly an encouraging scenario.

There may be a case for early combined treatment of depression with medications and psychotherapy [52,80] to improve acute and long term outcomes.

Research literature has paid particular attention to persistent sub threshold symptoms of depression [81]. These require due consideration as they can be linked with relapse. A combined treatment approach may well be more applicable here. The recent literature on mindfulness based cognitive therapy for depression has the potential for addressing this gap [59]. Routine psychological interventions do not have a conceptual approach to subsyndromal mood cycling whereas mindfulness approaches for depression are adapted to address this.

With psychopharmacological treatments it is easier to apply results of clinical trial to practice but fidelity to psychological treatment may be a challenge in routine practice. This may affect

outcomes such that they may be inferior to that achieved in clinical trials [82].

Given the rising evidence base for guided selfhelp in mild to moderate depression [83], there is opportunity to make this available cheaply and with high fidelity.

### Co-morbidity issues

Rise in life expectancy is increasing the burden of chronic illness and therefore the spectre of co-morbidity is growing [84]. Physical chronic conditions already have well established evidence based pathways for treatment however there is a glaring gap of guidelines where co-morbid chronic diseases are concerned [85].

Depression's co-morbidity with anxiety can affect treatment outcomes [86]. However detection of anxiety may provide the scope to integrate evidence based psychological intervention like CBT early. The co-morbidity with alcohol and substance use can be problematic. The good news is that depression in co-morbid conditions also responds to standard treatment [87,88]. Co-morbidity with physical health problems is another concern as it has reciprocal effect on outcomes of both depression and physical health conditions as discussed earlier.

A systematic approach to target co-morbidity in depression is needed. The term systematic refers here to a health system priority, given that depression contributes highest to the burden of disability. Such an approach would require interconnection and liaison between services create to enhance the treatment of depression.

### Post treatment issues

This is contradiction in terms as there is no post treatment phase for a long term condition. It is really a matter of continuity of treatment. In current practice maintenance antidepressants, routine follow ups and recognizing early warning signs is the best we have. There are many more options.

A systematic approach to management of the inter episode periods is largely missing in depression management even though there are interventions which have been researched. Mindfulness approaches can be used for relapse prevention. Since it is a group intervention, the cost is likely to be low. Early detection is critical and routine depression questionnaire with high sensitivity may be advantageous in identifying recurrence. Targeted booster CBT may also be considered and research into delivering this as low cost, easily disseminated guided self-help is sorely needed. Finally the key issue of antidepressant medication adherence must be addressed by a variety of means like patient and family education, telephone and text message reminders, self help programmes and connection to peer support groups. More research is needed to enhance adherence in long term conditions as a systematic review of interventions showed inconsistent effectiveness [89].

### System issues

Long term condition management is -truly speaking -not just a clinical approach but also a systems approach. This requires an efficient network of relevant information which is easily accessible to inform decision making. Current patient health record systems are designed to replace paper notes or serve the purpose of governance

and documentation as their primary goal. This needs to change. The primary goal of health care records should be to track clinical and functional outcomes such that management of those conditions is improved. Documentation, event monitoring, billing and scheduling are merely operations to achieve healthcare outcomes and not goals in themselves.

With specific reference to depression (and in fact most chronic conditions) the system must accommodate patient self-monitoring and tracking as this is key to detecting early relapse. Smart phone assisted technology is available to enhance chronic conditions management [90] but not yet integrated in healthcare systems. We already have technology delivered guided psychological treatments through such devices [91].

Recurrent depression registers which provide a unique code for healthcare management and communication may offer yet another way to track outcomes and provide treatment based on evidence based algorithm in primary care and specialist settings. This can also be combined with depression decision support systems to guide practitioners choose effective interventions.

Effective communication between healthcare providers especially with respect to critical health events changed the landscape of chronic disease management. A red flag approach for depression relapse is also feasible.

### Summary

Major depression has high likelihood of being a recurrent condition and as such requires a long term strategy for management. Disability due to depression can also persist in the long term. Chronic conditions management has made large strides in the last decade and clinical trials of this approach in depression are also effective. Whilst pharmacological recommendation for treatment of depression adopts a more long term treatment approach, the public education on depression is focused on acute treatment. This has to change. Non adherence to medication is very high in depression and health services do not offer a systematic approach to symptom monitoring and medication adherence. Psychological treatments are beginning to focus on the longitudinal course of depression rather than immediate symptom reduction. This is good news. A systems approach involving use of current technology can offer very promising directions in long term management of depression.

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