



Research report

## Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. II. Psychotherapy alone or in combination with antidepressant medication

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### ABSTRACT

**Background:** In 2001, the Canadian Psychiatric Association and the Canadian Network for Mood and Anxiety Treatments (CANMAT) partnered to produce evidence-based clinical guidelines for the treatment of depressive disorders. A revision of these guidelines was undertaken by CANMAT in 2008–2009 to reflect advances in the field. This article, one of five in the series, reviews new studies of psychotherapy in the acute and maintenance phase of MDD, including computer-based and telephone-delivered psychotherapy.

**Methods:** The CANMAT guidelines are based on a question–answer format to enhance accessibility to clinicians. Evidence-based responses are based on updated systematic reviews of the literature and recommendations are graded according to the Level of Evidence, using pre-defined criteria. Lines of Treatment are identified based on criteria that included evidence and expert clinical support.

**Results:** Cognitive-Behavioural Therapy (CBT) and Interpersonal Therapy (IPT) continue to have the most evidence for efficacy, both in acute and maintenance phases of MDD, and have been studied in combination with antidepressants. CBT is well studied in conjunction with computer-delivered methods and bibliotherapy. Behavioural Activation and Cognitive-Behavioural Analysis System of Psychotherapy have significant evidence, but need replication. Newer psychotherapies including Acceptance and Commitment Therapy, Motivational Interviewing, and Mindfulness-Based Cognitive Therapy do not yet have significant evidence as acute treatments; nor does psychodynamic therapy.

**Limitations:** Although many forms of psychotherapy have been studied, relatively few types have been evaluated for MDD in randomized controlled trials. Evidence about the combination of different types of psychotherapy and antidepressant medication is also limited despite widespread use of these therapies concomitantly.

**Conclusions:** CBT and IPT are the only first-line treatment recommendations for acute MDD and remain highly recommended for maintenance. Both computer-based and telephone-delivered psychotherapy—primarily studied with CBT and IPT—are useful second-line recommendations. Where feasible, combined antidepressant and CBT or IPT are recommended as first-line treatments for acute MDD.

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### Introduction

The Canadian Psychiatric Association and the Canadian Network for Mood and Anxiety Treatments (CANMAT), a not-for-profit scientific and educational organization, collaborated

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on the publication in 2001 of evidence-based clinical guidelines for the treatment of depressive disorders (Kennedy and Lam, 2001). A revision of these guidelines was undertaken by CANMAT in 2008–2009 to update the recommendations based on new evidence. The scope of these guidelines encompasses the management of adults with unipolar major depressive disorder (MDD). This section reviews psychotherapy, alone and in combination with medication, while a series of 4 companion sections review other aspects of MDD. There are separate CANMAT guidelines for Bipolar Disorder (Yatham et al., 2009).

Psychotherapy refers to the treatment of psychiatric and behavioural disorders through a method of communicating that invokes a psychological model of illness. This method of communication begins with a patient who seeks alleviation of current symptoms or prevention of recurrence of symptoms. Historically this required the establishment of a professional relationship between a patient and a therapist; with the advent of computer, internet, self-help, and to a lesser extent telephone therapies, the relationship is more explicitly between the patient and the psychological model, with an implicit link to the ‘therapist’ who designed the therapy.

Psychotherapy predates somatic therapies and includes a host of models, several of which have been rigorously tested, specifically for MDD. This review summarizes depression-specific psychotherapies as well as newer therapies which are promising, and seeks to clarify the evidence and usefulness of each major psychotherapy. While most psychotherapies share many common elements, the major treatments for MDD may be characterized by a number of key components: (a) the goal of treatment is alleviation of the core symptoms of depression, (b) there is careful attention to a specific method to deliver the therapy (typically a manual), (c) the psychotherapy focuses on the current problems of the patient, (d) high levels of activity are expected both of the therapist and the patient (who frequently has ‘homework’), (e) careful symptom monitoring, preferably with rating scales, is expected, (f) psychoeducation about the illness is a universal component, and (g) the treatment is generally time-limited, often paralleling the time course for pharmacotherapy. Furthermore, many of these therapies have been modified to be delivered in a group format. While a group approach may allow for integration of new techniques involving peer feedback and may be more cost-effective, the core of the psychotherapy remains unchanged, so group interventions are not evaluated in these guidelines as a separate “group therapy”. Similarly, context-specific therapies (such as marital therapy for MDD coinciding with a severe marital dispute) are not evaluated, since such therapies do not generalize to the average person with depression. Indications for a specific therapy, and the choice of either psychotherapy or pharmacotherapy alone or in combination are reviewed in a number of the following questions. The recommendations are presented as guidance for clinicians who should consider them in the context of individual patients, and not as standards of care.

## Methods

The full methods have been described elsewhere (Kennedy et al., 2009) but, in summary, relevant English language

publications from January 1, 2000 to December 31, 2008 were identified using computerized searches of electronic databases (PubMed, PsychInfo, Cochrane Register of Clinical Trials), inspection of bibliographies, and review of other guidelines and major reports. The previous question–answer format has been retained based on feedback from clinicians. Recommendations for each Line of Treatment are based on the Level of Evidence and clinical support (Table 1). A first-line treatment represents a balance of efficacy, tolerability and clinical support. Second-line and third-line treatments are reserved for situations where first-line treatments are not indicated or cannot be used, or have not worked.

CANMAT recognizes that much of the evidence is based on studies using strict inclusion/exclusion criteria with intensive and frequent follow up for a short duration of treatment, and therefore may not be applicable to the average patient seen by clinicians. Hence, there are few absolute recommendations and these guidelines should be viewed as guidance that must be tailored to an individual patient, and not as standards of care.

### 2.1. When is psychotherapy indicated for treatment?

Many factors influence the decision of when and where to employ psychotherapy. Employing a broad perspective, there are patient, provider, and (health) system issues that each play a role. Among the patient factors are adequacy of clinical evidence for a specific patient population (e.g. women during pregnancy); medication contraindications; patient preference; and the ability of a patient to engage in treatment. Patient preferences may in turn be influenced by social or cultural convictions regarding the efficacy of particular non-medical therapies, and the fear of potential medication side

**Table 1**  
Criteria for level of evidence<sup>a</sup> and line of treatment<sup>b</sup>.

Level	Criteria
1	At least 2 RCTs with adequate sample sizes, preferably placebo-controlled, and/or meta-analysis with narrow confidence intervals.
2	At least 1 RCT with adequate sample size and/or meta-analysis with wide confidence intervals.
3	Non-randomized, controlled prospective studies or case series or high quality retrospective studies.
4	Expert opinion/consensus.
Line of treatment	Criteria
First-line	Level 1 or Level 2 evidence, plus clinical support <sup>c</sup>
Second-line	Level 3 evidence or higher, plus clinical support <sup>c</sup>
Third-line	Level 4 evidence or higher, plus clinical support <sup>c</sup>

<sup>a</sup> Note that Levels 1 and 2 evidence refer specifically to treatment studies in which randomized comparisons are available. Recommendations involving epidemiological or risk factors primarily arise from observational studies, hence the highest level of evidence is usually Level 3. Higher order recommendations (e.g., principles of care) reflect higher level judgment of the strength of evidence from various data sources, and therefore are primarily Level 4 evidence.

<sup>b</sup> A first-line treatment represents a balance of efficacy, tolerability and clinical support. Second-line and third-line treatments are reserved for situations where first-line treatments are not indicated or cannot be used, or when first-line treatments have not worked.

<sup>c</sup> Clinical support refers to application of expert opinion of the CANMAT committees to ensure that evidence-supported interventions are realistic in clinical practice. Therefore, treatments with higher levels of evidence may be downgraded to lower lines of treatment due to clinical issues such as side effect or safety profile.

effects. Provider factors include the ability to provide the chosen psychotherapy of sufficient quality and in sufficient quantity to meet patient needs, as well as the capacity to engage the patient. System factors include ease of availability and if applicable, cost. System factors also play a role in which therapies are provided: some systems provide paid coverage for traditional psychotherapies such as psychodynamic methods for historical reasons, while other systems facilitate treatments that can be provided by specific professional groups within the health care system—for instance, the provision of CBT by specially trained counselors.

For the clinician using these guidelines, it would be reasonable to begin by identifying the first-line psychological treatments recommended for MDD, clarifying if there are any particular recommendations for a special subpopulation, and evaluating how the evidence and availability for these treatments compare to the evidence and availability of somatic therapies. Severity is another overarching issue in considering whether to recommend psychotherapy: for the most severe depressions, the efficacy and speed of somatic therapy over psychotherapy is a consideration.

Safety and relative contraindications should also be considered; it would be unwise to recommend monotherapy with psychotherapy in a severely suicidal patient, and the presence of psychotic depression would be an instance where psychotherapy alone would be contraindicated. While it is intuitive to assume that the combination of psychotherapy and pharmacotherapy may be better than either treatment alone, the strength of evidence varies across therapies, and availability issues often preclude combined treatments. Table 2 summarizes the treatment recommendations for psychotherapy for MDD. Since many psychotherapies exist, only those specifically studied for MDD are included, along with selected other forms which have significant prominence (e.g. Motivational Interviewing).

## 2.2. What is Cognitive-Behavioural Therapy (CBT)?

CBT for depression is an intensive, time-limited, symptom focused psychotherapy built on the premise that distorted beliefs about the self, the world, and the future maintain depressive affect. Once patients learn to recognize these automatic thinking patterns, they are taught more adaptive ways of responding. Behavioural interventions in CBT are

especially effective for symptoms of social withdrawal and anhedonia, and focus on activating patients' engagement in their environment as well as increasing their feelings of mastery and pleasure. These skills, when accompanied by affective arousal and practiced in the context of extra therapy assignments, are important engines of symptom change. As with other brief therapies, coverage of didactic content combined with case supervision is necessary to achieve competence in this approach. Further information can be obtained through the Academy of Cognitive Therapy's website ([www.academyofct.org](http://www.academyofct.org)).

## 2.3. How effective is CBT in acute MDD?

Evidence from 85 randomized controlled trials (RCTs) since 1977 provides empirical support for CBT's efficacy in treating MDD (mild to moderate in severity), with the modal finding being one of relative equivalence to antidepressant medication (effect size 0.38) for the acute phase episode and superiority over control conditions (effect size 0.82 against placebo and wait-list controls) (Gloaguen et al., 1998). An important extension of this work involves the treatment of more severely (but non-psychotic) depressed patients, with two studies finding no difference between CBT and antidepressant medication (DeRubeis et al., 2005; Luty et al., 2007). Further evidence for the comparability of CBT to pharmacotherapy is found in the results from the STAR\*D project, where CBT was one of several second level options for outpatients who failed to achieve remission with citalopram. For patients who switched to CBT there were no significant differences in remission rates and fewer side effects compared to switching to a different antidepressant, although the mean time to remission was approximately 3 weeks longer with CBT than with medication (Thase et al., 2007).

Additional extensions include recent evidence of the effectiveness of CBT in treating specific subgroups, for instance low income, young minority women (Miranda et al., 2003). A final factor influencing effectiveness of treatments is comorbidity, which is common in MDD. There is inconsistent evidence about the influence of comorbid personality disorders on psychiatric outcomes. With respect to patient selection, Joyce et al. (2007) compared CBT and IPT outcomes in depressed patients with comorbid personality disorder (PD) or traits and found that the presence of PD did not diminish clinical outcomes. In summary, there is Level 1 evidence for CBT in acute MDD, and it is a first-line treatment.

## 2.4. How effective is CBT in the maintenance phase of MDD?

This question deals with prevention of relapse following a successful acute treatment, and the ability of 'maintenance' or 'continuation' CBT to confer added benefits. A recent meta-analysis of 28 studies suggests that CBT prophylaxis endures beyond treatment cessation; if both CBT and medication are stopped after successful acute treatment of several months, patients who initially received CBT have lower rates of relapse (Vittengl et al., 2007). However, stopping acute phase CBT results in a relapse rate of 54% within 2 years (Vittengl et al., 2007); therefore, meta-analysis also examined the impact of maintenance CBT, using those who had already responded to CBT. The meta-analysis

**Table 2**  
Recommendations for individual psychotherapies for acute MDD.

First-line treatments	Cognitive-Behavioural Therapy [CBT; Level 1] Interpersonal Therapy [IPT; Level 1]
Second-line treatments	Bibliotherapy [Level 1] Behavioural Activation [Level 2] Cognitive-Behavioural Analysis System of Psychotherapy [CBASP; Level 2 evidence for chronic MDD with acute episode] Computer-assisted CBT [Level 2] Telephone-delivered CBT and IPT [Level 2]
Third-line treatments	Acceptance and Commitment Therapy [ACT; Level 3] Motivational Interviewing [Level 4] Psychodynamic therapy [Level 2] Emotion-Focused Therapy [Level 2]

used an “enriched design” by looking only at full responders, much like medication studies, but nonetheless revealed that maintenance CBT (often at a dose of one session per month) provided further protection against relapse, comparable to pharmacotherapy. There is also evidence that CBT provides continued protection against relapse after maintenance CBT is stopped: the relapse rate was 31% over the subsequent 12 months for patients who received acute CBT plus up to 3 maintenance sessions compared to a 76% relapse rate following medication withdrawal in remitted patients. However, if the medication patients received ongoing pharmacotherapy, relapse rates were similar (Hollon et al., 2005). Paykel et al. (2005) reported that the benefits of CBT prophylaxis in the context of combination treatment of residual depression continued for 4.5 years post CBT. What is not known is whether these effects are due to changes in the causal processes that contribute to relapse risk, or to the incorporation of compensatory strategies that neutralize their effects on mood regulation. Overall, there is Level 1 evidence, and CBT is recommended as a first-line treatment for the maintenance phase of MDD.

### 2.5. What is Interpersonal Therapy (IPT)?

Interpersonal Psychotherapy (IPT) is a time-limited, manualized psychotherapy, that was first developed in the 1970's for the outpatient treatment of individuals with MDD. Much like the adaptation of CBT to treat other disorders, IPT has been modified for the treatment of Eating Disorders, Dysthymia, Bipolar Disorder, Substance Use Disorder, Panic Disorder, Social Anxiety Disorder, Body Dysmorphic Disorder, Somatization and Borderline Personality Disorder. IPT deals with current interpersonal relationships and focuses on the immediate social context. The original IPT format involved 16 sessions with three phases and a focus on one or more areas including role transitions, interpersonal role disputes, grief or interpersonal deficits; these foci have been modified for application in special populations. Numerous training options exist and information can be obtained on the International Society for Interpersonal Psychotherapy website (isiIPT, [www.interpersonalpsychotherapy.org](http://www.interpersonalpsychotherapy.org)).

### 2.6. How effective is IPT in MDD?

Among the many meta-analyses and reviews of IPT, two provide more specific overviews of the precise targeting of MDD (Markowitz, 2008; Parker et al., 2006). Although one meta-analysis did find IPT superior to CBT (deMello et al., 2005) and another reported modest superiority of antidepressant

medications over IPT (effect size 0,15) (Kotova, 2005), the weight of evidence does not support the superiority or inferiority of IPT compared to CBT or pharmacotherapy. Combination treatment with IPT and medication has not been found to be superior to either alone (Barkham and Hardy, 2001; Kotova, 2005; deMello et al., 2005). Important extensions of IPT include studies of acute and maintenance treatment of elderly patients, acute treatment for adolescents, several group studies with heterogeneous populations, and in prevention of MDD in high risk groups (Roth and Fonagy, 2005). There is Level 1 evidence for IPT as a first-line treatment recommendation for acute MDD, and Level 2 evidence for IPT as a second-line treatment recommendation for the maintenance phase of MDD (see Table 3).

### 2.7. What is psychodynamic therapy?

Psychodynamic psychotherapy is based on psychoanalytic principles (Bond, 2006). At its core is the assumption that conscious or unconscious emotions and defence mechanisms can contribute to the development of negative emotional and cognitive states, including those associated with MDD and anxiety disorders. By developing insight into these factors, i.e. recognizing them and understanding their source and influence on behaviour as well as physical and mental symptoms, psychological healing can take place. The therapeutic relationship plays a key role in the process.

### 2.8. How effective is psychodynamic psychotherapy?

Complicating factors in the evaluation of efficacy include combination of both short-term and long-term interventions under a single umbrella of psychodynamic therapy and the inclusion of broadly defined patient groups—often having a mix of significant depressive and anxiety symptoms—rather than definite MDD. Furthermore, psychodynamic therapy studies often lack the specific symptom measures established as valid outcome measures for almost all other treatments; this weakens the ability to support psychodynamic therapy as evidence-based. As noted in the previous guidelines (CANMAT, 2001), a meta-analysis found brief psychodynamic psychotherapy superior to no treatment in MDD, but inferior to alternate therapies like CBT (Svartberg and Stiles, 1991). However, these authors included IPT as a psychodynamic psychotherapy. Since 2001, psychodynamic psychotherapy has been evaluated in mild to severe MDD (with or without comorbid personality disorders), dysthymia, “double depression” and post partum depression (e.g. Burnand et al., 2002; Cooper et al., 2003;

**Table 3**  
Recommendations for major psychotherapies for MDD.

Comparison of evidence for CBT and IPT and other major psychotherapies				
	CBT	IPT	Psychodynamic psychotherapy	Behavioural activation
Acute MDD	First-line treatment [Level 1]	First-line treatment [Level 1]	Third-line treatment [Level 2]	Second-line treatment [Level 2]
Maintenance	First-line treatment [Level 1]	Second-line treatment [Level 2]	Lack of specific findings with respect to MDD do not allow for recommendation	Second-line treatment [Level 2]
Combination with medications	Second-line treatment [Level 1]	Second-line treatment [Level 1]	Insufficient evidence	Insufficient evidence

Trowell et al., 2007; Wilson et al., 2008). The inclusion of diverse patient populations and treatment models (e.g. short psychodynamic supportive psychotherapy, brief/short-term psychodynamic therapy) further limits conclusions about the effectiveness of psychodynamic psychotherapy.

Formal meta-analyses comparing psychodynamic therapy to cognitive-behavioural or behavioural interventions (CBT/BT) have yielded mixed results, with two reporting that psychodynamic therapy is as effective as CBT/BT (Leichsenring, 2001; Wilson et al., 2008 in older adults), and one reporting that CBT is superior (Pinquart et al., 2007, in older adults). However, the Leichsenring study (2001) found only six suitable trials for inclusion, and noted that there were “no two studies of independent research groups demonstrating equal effectiveness of the same form of short-term psychodynamic psychotherapy (STPP) compared to CBT/BT in the treatment of depression.” Given the heterogeneity of treatment models, durations, and types of populations, even under the rubric of ‘short-term’ psychodynamic psychotherapy, these studies provide Level 2 evidence and are recommended as third-line interventions (Anderson and Lambert, 1995). In patients with complicated comorbidities including personality disorders, however, there is Level 2 evidence to recommend psychodynamic therapy as a second-line treatment (Kool et al., 2003; Abbas, 2008; Bond and Perry, 2006).

### 2.9. How effective is psychodynamic psychotherapy in the maintenance phase of MDD?

There are only preliminary systematic outcome data on the long-term benefits of psychodynamic psychotherapy. Although one meta-analysis evaluated treatments longer than 1 year for a variety of disorders that included MDD and found benefit in general, it did not specify findings explicitly for MDD alone. As a result, the lack of evidence does not allow for recommendation of the value of psychodynamic psychotherapy for prevention of relapse of MDD (Leichsenring and Rabung, 2008).

### 2.10. Does psychotherapy prevent relapse in MDD?

The goals for any therapeutic intervention encompass both acute phase remission and maintenance phase prevention of relapse/recurrence. This has bolstered the use of

psychotherapy as a continuation or maintenance treatment, as summarized in Table 4. Additionally, issues with non-adherence and other barriers to continuation therapy with antidepressants support the role of psychotherapy to prevent relapse. Furthermore, even continuation pharmacotherapy does not prevent all relapses of MDD, reinforcing a possible role for psychotherapy. Overall, data from depression-specific psychotherapies support their utility in preventing episode return; too few studies exist to evaluate similar benefits from long term psychodynamic treatments. Rates of relapse following acute phase CBT are similar to those for patients continuing on antidepressants (Hollon et al., 2005), while remitted patients receiving maintenance IPT (M-IPT) or CBASP (Klein et al., 2004) during remission benefit more than those who receive clinical management. Monthly M-IPT was as effective as weekly or biweekly sessions in patients who remitted with IPT alone, but less effective for patients who required SSRI augmentation to achieve remission (Frank et al., 2007; Browne et al., 2002). Psychological strategies have also been applied to enhance medication adherence (Dotoli et al., 2006) with fewer relapses following fluvoxamine and group psychoeducation compared to patients treated with fluvoxamine alone; however, a comprehensive review by Vergouwn et al. (2003) noted that improved antidepressant adherence in primary care was not achieved by psychoeducational interventions alone, but was achieved when multifaceted interventions including psychoeducation were provided.

Beyond enhancement of adherence and the continuation of acute depression psychotherapy into the maintenance phase, specific psychotherapy approaches have been designed to be sequenced with pharmacologically-induced remission. Fava et al. (2004) developed a modified CBT to include a “Well Being” focus on lifestyle management as well as affective symptoms (CBT-WB). Recurrent depressed patients who were treated to remission pharmacologically and withdrawn had a 90% relapse rate over 6 years, compared to a rate of 40% for patients who received CBT-WB following drug discontinuation. Similarly, Mindfulness-Based Cognitive Therapy (MBCT), a group intervention that targets dysphoria-activated depressogenic thinking has been evaluated in remitted, recurrently depressed patients. Controlled clinical outcomes for MBCT indicate increased relapse-free survival time by 50% in unmedicated patients, compared to patients receiving treatment as usual. In addition, depressed patients who remitted with pharmacotherapy and who were discontinued onto MBCT had the same rate of relapses as patients who continued antidepressant medication (Kuyken et al., 2008). These results provide additional evidence that several psychotherapy approaches may reduce relapse in MDD. While the presence of several RCTs provide Level 1 evidence, the diversity of psychotherapy models and small number of study participants indicate a second-line treatment recommendation.

### 2.11. What is Motivational Interviewing?

Motivational Interviewing (MI) was originally developed by Miller (1996) as a strategy for engaging and treating patients with substance use disorders (SUDs). MI incorporates the levels of motivation outlined in Prochaska and DiClemente's (1986) stages-of-change model. MI is a person-centred clinical method

**Table 4**

Recommendations for individual psychotherapies for maintenance phase of MDD.

First-line treatments	CBT [Level 1]
Second-line treatments	Behavioural Activation [Level 2] CBASP [Level 2] IPT [Level 2] MBCT [Level 2]
Third-line treatments	None with evidence
Insufficient evidence to make a recommendation	ACT Motivational Interviewing Psychodynamic therapy Emotion-Focused Therapy Bibliotherapy Computer-assisted Telephone-delivered

to help patients resolve ambivalence and move ahead with change. Although it has been applied as a preparation for treatment and a freestanding brief intervention for SUDs, the term has also been used to describe a clinical style, and a default approach when motivational obstacles are encountered in treatment. MI approaches have been found to be equivalent to other active treatments for substance related disorders and have yielded moderate effects (0.25–0.57) compared to no treatment or placebo (Burke et al., 2003). MI has been incorporated into evidence-based therapy such as CBT for depression for those who are ambivalent about change and about taking necessary actions to bring about change.

### 2.12. How effective is Motivational Interviewing for MDD?

No published trials were identified using MI alone in patients with a primary diagnosis of MDD. Five MI trials involving subjects with a primary SUD also included some subjects with either depressive symptoms or full MDD, and found reductions in both substance misuse and depressive symptoms. For example, Baker et al. (2006) randomized 65 subjects with substance abuse and a psychotic disorder to a 10 session intervention which consisted of MI and CBT and compared them to 65 subjects who received routine treatment; the intervention showed short-term improvement in depression scores. Individuals with more severe depression benefited from more sessions (Baker et al., 2005). The general strategies of MI appear to increase the chances of successful treatment for the SUD and may also maximize the dual diagnosis patient's participation in treatment, and improve outcome. Thus, it is unclear if the improvement in substance abuse is a result of the impact of MI on the depression or independent of it. In the absence of specific MDD studies, evidence is at Level 4 (expert opinion) and MI receives a third-line recommendation.

### 2.13. What is Cognitive-Behavioural Analysis System of Psychotherapy (CBASP)?

CBASP is a form of psychotherapy that was developed specifically for the treatment of chronic depression (Arnow, 2005; McCullough, 2003; Swan and Hull, 2007). It involves cognitive, behavioural and interpersonal strategies and is focused on helping patients to recognize how maladaptive cognitions and behaviours influence each other and lead to and perpetuate negative outcomes. These outcomes include negative relationship patterns, which are seen as a particular difficulty for chronically depressed patients. The therapeutic relationship serves as a medium for negative interpersonal behaviours to be changed.

### 2.14. How effective is CBASP for acute MDD?

Although there have been 11 publications on the efficacy of CBASP in chronic depression since 2000, they all relate to the same large multi-centre clinical trial, first reported by Keller et al. (2000) that was referenced in the previous guidelines (CANMAT, 2001). In this study, combination therapy was significantly superior to either treatment alone in improving symptoms and psychosocial functioning. The combination was also associated with significantly less attrition and significantly greater maintenance of gains during continuation treatment,

though the individual treatments were also effective (Arnow et al., 2007; Hirschfeld et al., 2002; Keller et al., 2000; Kocsis et al., 2003; Rush et al., 2005). However, nefazodone and combination therapy were superior to CBASP in improving sleep and sexual functioning (Manber et al., 2003; Thase et al., 2002; Zajecka et al., 2002). Regarding attrition, overall, CBASP and nefazodone had similar drop-out rates (Arnow et al., 2007), but when only monotherapy non-responders were considered, CBASP was associated with significantly lower attrition (Schatzberg et al., 2005). Finally, there was a significant advantage of CBASP, in monotherapy or combined with medication, compared to medication alone in a subset of patients who had experienced early childhood trauma (Nemeroff et al., 2003). In summary, there is Level 2 evidence to support CBASP as second-line monotherapy or “add-on” to antidepressants in the acute treatment of chronic MDD, with evidence of sustained benefit.

### 2.15. How effective is CBASP for maintenance therapy in MDD?

The evidence is derived from the extension phase of the previously described large scale acute treatment trial (Keller et al., 2000). In this continuation trial, CBASP alone and CBASP/nefazodone groups received 6 sessions of CBASP over 16 weeks and the combination group continued to demonstrate superior outcomes (Kocsis et al., 2003).

There was also a 1 year monotherapy treatment phase in which CBASP was found to be significantly superior for relapse prevention (Klein et al., 2004). Thus, Level 2 evidence also supports CBASP as second-line monotherapy or “add-on” to antidepressants in continuation and maintenance phases of treatment.

### 2.16. What is Acceptance and Commitment Therapy (ACT) and its efficacy?

ACT; Hayes et al., 2006) is a new model of psychotherapy stemming from CBT that is commonly referred to as a “third generation behaviour therapy” (along with Dialectical Behaviour Therapy and Mindfulness-Based Stress Reduction). ACT shares with CBT the grounding in empiricism and working within an active collaborative therapeutic relationship. ACT is based in a contextual theory of language and cognition (relational frame theory) (Barnes-Holmes et al., 2001). Many of the strategies used in ACT are borrowed from other models (use of metaphors and stories to communicate treatment concepts, behavioural exercises) that have been further refined and developed. Psychopathology is theorized to result largely from “experiential avoidance.” The aim is to increase acceptance of the full range of subjective experiences, including distressing thoughts, beliefs, sensations and feelings, and subsequently cultivate a mindful outlook (i.e., awareness of mental events as products of the mind rather than literal truths). Strategies are used in an effort to promote desired behaviour change and ultimately quality of life. The concept of committed action towards one's goals is promoted in the context of experiential acceptance.

ACT has been applied in such conditions as workplace stress, psychosis, test anxiety, trichotillomania, epilepsy, obsessive-compulsive disorder, social anxiety, chronic pain, smoking cessation, diabetes, and substance abuse (summarized in a meta-analysis by Hayes et al., 2006). There is only one published

RCT involving MDD patients among heterogeneous outpatients with depressive, anxiety and adjustment disorders who were randomly assigned to CT or ACT (mean 15 sessions for CT and 16 sessions of ACT). Although this trial lacked a placebo condition, both treatment groups showed a significant reduction in depressive symptoms but the mechanisms of action were found to differ (Forman et al., 2007). With Level 3 evidence, ACT is recommended as third-line treatment for MDD.

### 2.17. What is Behavioural Activation (BA) for depression and its efficacy?

Behavioural Activation Therapy (BA) is based on the premise that depression is a consequence of compromised environmental sources of positive reinforcement. Treatment involves increasing patient activity and access to rewarding experiences, evaluating the consequences of depressive versus non-depressive behaviours and de-emphasizing particular cognitions or mood states as necessary for re-engaging with one's environment. This approach is well suited to address the inertia, avoidance and social withdrawal faced by many depressed patients and it has been suggested that the narrower focus on activation strategies may aid its dissemination. In the first of two RCTs of MDD, three arms involved BA, CBT, and an "Automatic Thought" arm that involved BA plus some but not all aspects of classic CBT. That study randomized 150 subjects but did not have a control group; all three treatments were equivalent in the acute phase as well as in relapse prevention (Jacobson et al., 1996; Gortner et al., 1998). A subsequent RCT (Dimidjian et al., 2006) randomized 241 subjects to four conditions: CBT, BA, pharmacotherapy, and control, with a double blind phase for 8 weeks followed by open treatment for another 8 weeks. The authors identified "severe depression" as HAM-D > 19 and reported that both BA and medications outperformed CBT and placebo in this subpopulation. In a follow up to this study, treatment responders were divided into three groups: (i) those who had originally received BA or CBT (ii) subjects discontinued from antidepressants and (iii) subjects maintained on antidepressants. BA and CBT were comparable in preventing relapse, and equal to continuing medication; these three groups in turn had longer time to relapse than those in the medication discontinuation arm (Dobson et al., 2008). Together, this body of evidence supports the efficacy of BA in both acute treatment and relapse prevention, as a second-line treatment with Level 2 evidence (based on the relatively small number of subjects and the fact that substantially the same investigators conducted all the trials).

### 2.18. What is Emotion-Focused Therapy (EFT) and its efficacy?

Emotion-Focused Therapy is a relatively new short-term psychotherapy, with an MDD intervention that involves sixteen to twenty individual sessions (Greenberg, 2002). The goal of EFT is to help the individual express emotions more easily by promoting emotional processing that brings emotional memory into consciousness. For MDD, this entails changing the emotionally based organization of the self through a number of techniques including focusing on an unclear bodily felt sense, dialogue with one critical internal voice, and "empty-chair dialogue" with a significant other

regarding unresolved issues. Several small RCTs have been conducted using this technique, with various control conditions. One trial compared EFT to CBT and found equivalent improvement in acute MDD, while another found slight superiority to Client-Centred care (Watson et al., 2003; Goldman et al., 2006). In view of the trials emanating from substantially the same investigators and the small number of subjects, evidence is at Level 2 and the recommendation for EFT is as a third-line treatment.

### 2.19. What is bibliotherapy and its efficacy?

Bibliotherapy, the reading of self-help materials for psychological treatment, has numerous advantages over other treatments. It is self-paced, more convenient, less costly, and does not carry the stigma associated with attending a mental-health professional. On the other hand, the low motivation and energy experienced by depressed patients may compromise adherence. Nevertheless, bibliotherapy has received increasing attention, either as a stand-alone or combination treatment for a broad spectrum of mental health problems. Individuals opting for bibliotherapy assume greater responsibility for treatment and outcome, and thus have a greater sense of control; this is seen as a key feature of the management of chronic diseases like depression.

In an early meta-analysis of bibliotherapy for depression, summarizing RCTs where the control condition was usually assignment to a waiting list for treatment, a large overall effect size of 0.83 was found (Cuijpers, 1997). Research comparing bibliotherapy that uses cognitive techniques with bibliotherapy that uses behavioural techniques indicates no differences between treatments, with superior outcomes in both groups compared to control conditions (Scogin et al., 1989), echoing the research findings about BA and CBT delivered by a therapist. Looking strictly at books, a meta-analysis by Anderson et al. (2005) identified 11 RCTs testing efficacy. While many self-help books on MDD exist, eight of the trials utilized "Feeling Good" (Burns, 1980). The meta-analysis concluded that all of the RCTs were small and had other limitations, and hence claimed the efficacy overall was weak. A subsequent meta-analysis of 34 studies (Gellatly et al., 2007) found bibliotherapy still effective, but noted clinical heterogeneity in study participants, from subclinical to clinical MDD. Studies using subjects with lesser severity, and particularly those in trials with a wait list control, showed more effect. This review also noted significant benefit if the self-help strategy was augmented by a clinician providing guidance and encouragement. These findings and limitations in studies suggest a second-line recommendation for bibliotherapy, with encouragement of use of bibliotherapy as an adjunct to formal psychotherapy or medication.

### 2.20. How effective is computer-based/internet delivery of psychotherapy for MDD?

Four meta-analyses of computer-based psychotherapies have been published involving 20–73 different studies across various psychiatric disorders. More specifically, 8 RCTs have been published, mostly for patients with depressive symptoms rather than a diagnosis of MDD. A confounding factor is that some studies involve only internet therapy, some involve

accessing psychotherapy via a computer in a clinic, and some involve computer-based exercises with brief coaching from clinicians, either live or via email. As reviewed by [Spek et al. \(2007\)](#), a meta-analysis of 4 RCTs involving depressive symptoms identified small effect sizes for MDD but large effect sizes in a separate analysis of internet CBT for anxiety disorders. Key factors hindering evaluation of internet CBT involve the inclusion of mixed groups of individuals with depressive symptoms ranging from subclinical to full episode MDD, and outcome measures that show reduction in symptoms without reporting of remission or response rates in MDD. Furthermore, limited information is provided on participant satisfaction, although retention rates are noted to be low. Such findings need to be balanced by the remarkable accessibility and reach of such interventions, particularly in a climate of massive use of the internet for health and disease information ([Marks et al., 2003](#)). [Andersson et al. \(2005\)](#) reported results of an RCT with two arms: the active intervention consisted of internet-delivered CBT with minimal therapist contact and a moderated online discussion group, compared to a control group which received only a separate online discussion group. This study specifically targeted MDD, and showed a moderate effect size between intervention and control. In addition, several studies of purely computer-based CBT delivery systems used in doctors' offices provide further evidence. [Proudfoot et al. \(2004\)](#) conducted an RCT with 274 patients with symptoms of anxiety and/or depression, randomly allocated to receive computerized CBT, with or without medication, or treatment as usual, with follow up assessment at 6 months. The computerized therapy improved depression symptoms, negative attributional style, work and social adjustment, without interaction with drug treatment, duration of pre-existing illness or severity of existing illness. Together, these studies provide Level 2 evidence and a second-line recommendation for computer-based psychological interventions.

#### 2.21. How effective is telephone administered psychotherapy for MDD?

Telephone-based interventions for depression may be divided into two broad categories: telephone disease management and telephone psychotherapy. A large number of chronic disease management studies treating both depressive symptoms below MDD criteria and full MDD have used an element of telephone outreach to patients or providers; and in at least one study by [Datto et al. \(2003\)](#), telephone management was effective as the primary intervention. Advantages include immediacy of help, a degree of anonymity, low cost and ease of access.

In an RCT involving 600 MDD patients in primary care, [Simon et al. \(2004\)](#) evaluated three interventions: usual care, telephone care management (involving 3 phone calls to the patient, care coordination, and feedback to the physician) and telephone care management coupled with 8 sessions of CBT by phone. Those in the telephone CBT group showed significant improvement in depressive symptoms compared to those in usual care. The telephone management group did not demonstrate significant improvement in depressive symptoms, but patient self report of improvement and satisfaction with treatment were superior to usual care. Another RCT

involving MDD in individuals with Multiple Sclerosis ([Mohr et al., 2005](#)) showed the efficacy of a 16 session telephone CBT intervention. Several other studies have shown the acceptability and efficacy of telephone therapy ([Bee et al., 2008](#)). However, the studies are small and the types of therapy vary—IPT, CBT, supportive therapy—which make definitive conclusions difficult. In summary, while telephone-based interventions for depression are promising, they need to be studied further under more rigorous conditions; there is Level 2 evidence and clinical recommendation for their inclusion as second-line treatments.

#### 2.22. Is combined treatment with psychotherapy and medication superior to psychotherapy alone?

Combination treatment for MDD can be either sequential (e.g., acute medication for 8 weeks, followed by psychotherapy) or concurrent (starting both treatments at the outset), and is summarized in [Table 4](#). Evaluating outcomes of concurrent therapy is complicated by varying modes of delivery, including the use of single versus dual treatment providers. Perhaps because of these variations, results of initial meta-analyses were inconsistent and failed to provide evidence of superiority for combined treatment. However, a subsequent meta-analysis combining 18 studies with over 1800 subjects concluded that concurrent medication and psychotherapy was superior to psychotherapy alone, with a small to moderate effect size of 0.35 ([Cuijpers et al., 2009](#)). Most studies involved either CBT or IPT. Interestingly, when concurrent therapy is evaluated in more focal populations like the elderly, its superiority increases ([Cuijpers et al., 2009](#)).

#### 2.23. Is combined treatment with psychotherapy and medication superior to medication alone?

Combination treatment for depression has also been compared to medication alone. Most studies are small, so meta-analyses and systematic reviews of the area involve relatively small number of subjects. Furthermore, the issue is complicated by differing approaches to combined treatment—in particular, more studies involve a sequential rather than strictly concurrent treatment approach, and variability exists in treatment delivery: sometimes one therapist provides both treatments, sometimes separate providers deliver psychotherapy and medication. In a meta-analysis ([Pampallona et al., 2004](#)), sixteen studies assigned 932 patients to combined concurrent therapy versus 910 to medications alone; clear superiority was seen with combined concurrent therapy in terms of symptom reduction, and in studies longer than 12 weeks, patient drop-out rates were significantly reduced in the combined treatment group. These researchers were unable to clarify if simple enhanced medication adherence might have been the active ingredient of the psychotherapy. Another study with less conclusive demonstration of benefit of the dual therapy show striking preference of the patients for combined treatment ([de Jonghe et al., 2004](#)); since patient preference is a major concern in psychiatric treatment, this too needs consideration in treatment recommendations.

In conclusion, the evidence suggests that combined treatment is superior to pharmacotherapy alone, and these effects



**Table 5**

Considerations for combining psychotherapy and medication.

Concurrent combined treatment	<ul style="list-style-type: none"> <li>• Combined pharmacotherapy and CBT or IPT is superior to either modality alone, but the superiority is most evident in special populations such as the elderly or women. [Level 1]</li> <li>• Practical concerns including cost and availability may outweigh the additional benefit of concurrent combined treatment.</li> <li>• Both bibliotherapy and computer-assisted psychotherapy have evidence for efficacy, and may be particularly useful in combination with pharmacotherapy.</li> </ul>
Sequential combined treatment (start pharmacotherapy, add psychotherapy later)	<ul style="list-style-type: none"> <li>• Addition of psychotherapy (CBT or IPT) to partial responders to pharmacotherapy in the acute phase of MDD. [Level 2]</li> </ul>
Crossover treatment (acute pharmacotherapy followed by switch to psychotherapy when well for maintenance)	<ul style="list-style-type: none"> <li>• Discontinuing successful pharmacotherapy and crossing over to psychotherapy has never been shown to be superior to continuing pharmacotherapy.</li> <li>• Crossover to CBT, MBCT, or IPT in the absence of medication has been shown to provide significant benefit, with relapse prevention generally comparable to continuation of the pharmacotherapy. [Level 2]</li> </ul>

are more pronounced in relapse prevention than in symptom relief in acute treatment (6–8 weeks), as reviewed below. This Level 2 evidence, coupled with patient (and often provider) preference for combined treatment, suggest that combined treatment could be a first-line recommendation for MDD; however, issues including practicality, cost, and availability relegate this to a second-line treatment recommendation.

#### 2.24. Is sequential treatment (pharmacotherapy followed by psychotherapy) superior to monotherapy?

No meta-analysis specifically explored this question, perhaps since few studies specifically address this issue. This issue is complicated by different approaches to sequential treatment; in some cases, patients are treated to response or remission with pharmacotherapy before receiving psychotherapy as a maintenance phase intervention, primarily to prevent relapse; in others, only those patients who fail to respond to pharmacotherapy receive the addition of psychotherapy (Table 5). There is evidence that MBCT has efficacy in relapse prevention among patients with 3 or more previous episodes; however, the overall number of subjects was small and not all had pharmacotherapy in the acute phase (Coelho et al., 2007). A broader review of the role of psychotherapy in prevention of relapse is summarized in Question 10, but that review combines studies with and without pharmacotherapy. Paykel et al. (1999) examined the value of CBT delivered to patients with residual symptoms after pharmacotherapy and found that those who received CBT had further reduction of acute symptoms and reduced rates of relapse. Based on a review by Rafanelli et al. (2007), there is Level 2 evidence to support sequential treatment (pharmacotherapy followed by psychotherapy) of MDD, and this is considered a second-line recommendation.

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#### Conflict of Interest

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SHK is on Speaker/Advisory Boards for, or has received research funds from: Advanced Neuromodulation Systems Inc, AstraZeneca, Biovail, Boehringer-Ingelheim, Brain Cells Inc, Canadian Network for Mood and Anxiety Treatments, Eli Lilly, GlaxoSmithKline, Janssen-Ortho, Lundbeck, Lundbeck Institute, Merck Frost, Servier and Wyeth.

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