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Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea

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Although pharmacological treatment constitutes the main therapeutic approach for depression, non-pharmacological treatments (self-care or psychotherapeutic approach) are usually regarded as more essential therapeutic approaches in clinical practice. However, there have been few clinical practice guidelines concerning self-care or psychotherapy in the management of depression. This study introduces the 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea.' For the first time, a guideline was developed for non-pharmacological treatments for Korean adults with mild-to-moderate depression. The guideline development process consisted of establishing several key questions related to non-pharmacologic treatments of depression, searching the literature for studies which answer these questions, assessing the evidence level of each selected study, drawing up draft recommendation, and peer review. The Scottish Intercollegiate Guidelines Network grading system was used to evaluate the quality of evidence. As a result of this process, the guideline recommends exercise therapy, bibliotherapy, cognitive behavior therapy, short-term psychodynamic supportive psychotherapy, and interpersonal psychotherapy as the non-pharmacological treatments for adult patients with mild-to-moderate depression in Korea. Hence, it is necessary to develop specific methodologies for several non-pharmacological treatment for Korean adults with depression.

Keywords: Depression; Non-Pharmacological Treatment; Self-Care; Psychotherapy; Guideline; Korea

INTRODUCTION

Depression is a highly prevalent psychiatric disorder that tends to be recurrent and chronic (1). World Health Organization (WHO) has predicted that depression will be the second leading cause of early death or disability by 2020 (2). In Korea, depression is a prominent social issue, as suicidal rates have rapidly increased after the year 2000 (3). Nevertheless, clinical treatment for depression had not been standardized and is usually dependent on the clinical experiences or decisions of individual psychiatrists. Since the late 1990s, several mental health groups in Korea have developed evidence-based clinical practice guidelines in order to provide an organized systemic review of therapeutic recommendations for depression (4, 5).

The Korean Guideline Development Team for Depression considered the minimal infrastructure needed to develop an evidence-based clinical practice guideline for depression in Korea. The group was encouraged by the improving research environment in which the communication network provided up-to-date knowledge of depression treatment (6). By 2005, the Ministry of Health and Welfare, Republic of Korea Government took note of depression as a serious public health issue and considered a clinical practice guideline for depression to be essential to improve and organize its treatment or management. Eventually, the Ministry founded the Clinical Research Center for Depression as a project to develop the infrastructure of public mental health and medical management for depression (7). The Clinical Research Center for Depression aimed to identify the natural history of disease through clinical studies in Korean adults with depression and made a Korean version of an evi-

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dence-based treatment guideline for depression. By 2006, the necessity for a non-pharmacological treatment guideline for depression was confirmed through 'Investigation of the Current Status and Requirement of Non-Pharmacological Treatment for Depression in Korea' by the Third Detailed Task Force of the Clinical Research Center for Depression. In this investigation, 236 consecutive outpatients with depression in Korea were recruited in 12 university-affiliated hospitals. The depressed patients filled out a self-report questionnaire about current clinical status and non-pharmacological treatment for depression. Specifically, the questionnaire composed of 19 questions concerning desired type of depression treatment by patients, desired length and cost of psychiatric interviews by patients, means of obtaining information about depression, and other matters relating to psychiatric care. When asked about the goal of treatment for depression, 75.5% of patients answered that the goal to be improvements in physical and affective symptoms, but 24.5% desired a higher level of treatment goal including reformulation of personality or resolution of inner conflicts. When asked about sources of information regarding depression, 60% of patients referred to individual clinical psychiatrists while 18.9% cited mass media. These findings indicated that non-pharmacological approaches for depression were necessary and also that clinical psychiatrists required a clinical practice guideline for depression (8).

Although the basic therapeutic approach for depression is pharmacological treatment, clinical psychiatrists considered that non-pharmacological approaches were more essential. However, non-pharmacological treatment guidelines had not been developed in Korea at that time. Hence, the Development Group of the Standardized Treatment Guideline for Depression of the Clinical Research Center for Depression, assigned by the Ministry of Health and Welfare, hoped that the present guideline would promote non-pharmacological approaches to provide alternative or adjuvant therapeutic mode of depression. Since relatively more severe depression essentially requires pharmacological treatment, pharmacological guidelines focus on patients with moderate or severe depression (7). However, according to severity classification of major depressive disorder of the DSM-IV (9), relatively less severe depression can be managed through non-pharmacological approaches. Thus, the 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea' has been indicated to the Korean adults with mild or moderate depression. We described below a summary of the guideline, which has been developed according to a strict and systematic process using an evidence-based approach.

MATERIALS AND METHODS

Development group

The Development Group for the Standardized Treatment Guideline for Depression was formed as a multidisciplinary team consisting psychiatrists, administrative researchers, clinical psychologists, systematic review experts, and specialists in preventive medicine. Throughout the process of developing the clinical practice guideline, members of the group carried out ongoing comparative assessment and evaluation of all results while performing the investigations and procedures required in order to base the findings on scientific methodology (8).

Range of the guideline

The Development Group investigated pre-existing domestic and international treatment guidelines, as well as trends in the management of depression among Korean psychiatrists. Subsequently, the Development Group analyzed the results of previous investigations (10-50) and developed a non-pharmacological treatment guideline for depression. The Development Group also assessed the domestic status of depression treatments in Korea. The 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea' was indicated at Korean adult patients with an initial diagnosis of mild or moderate depression by DSM-IV (9).

Key questions

Common self-care methods for depression include bibliotherapy, computer-based treatment, dietary supplements (St. John's wort, S-adenosylmethionine, selenium, vitamin B, C, D, folic acid, Ginkgo biloba, glutamine, tyrosine, natural progesterone, oriental medicine, caffeine, alcohol, omega-3 fatty acids, and others), acupuncture therapy, light therapy, anion therapy, massage therapy, exercise therapy, relaxation therapy, music therapy, hypnotherapy, yoga, meditation, and aromatherapy (51). Among these, the literature evidence was the most convincing for St. John's wort, exercise therapy, bibliotherapy, and light therapy during the winter. In the context of domestic situation in Korea, exercise therapy and bibliotherapy were considered to be worthy of recommendation as first stage of treatments for mild or moderate depression. St. John's wort was not included in this guideline, since it is classified as not a Over-the-Counter (OTC) drug but a prescription medication in Korea. Light therapy was also excluded, because it is not widely clinically-available in Korea. In addition to self-care methods, this guideline addressed psychotherapy methods. For any form of psychotherapy, it is important to consider whether a given method has independent and well-established therapeutic features that justify the title of 'psychotherapy' because an unverified psychotherapy is nothing but a placebo treatment. According to Wampold et al. (52), psychotherapy should have the following key elements to be distinguished from general clinical management or a placebo treatment. First, the therapy is mediated by a trained specialist. Second, the therapist can carry out treatments tailored to the needs of each patient. Third, there should be a

unique and clear psychotherapeutic principle that distinguishes it from other forms of psychotherapy. From this viewpoint, only a few kinds of psychotherapy are comparable to pharmacological treatments or placebo controls. These are cognitive-behavioral therapy (CBT), short-term psychodynamic supportive psychotherapy (SPSP), interpersonal psychotherapy (IPT), problem-solving treatment, and marital therapy. Among these, the guideline evaluated three psychotherapies, namely CBT, SPSP, and IPT because these three methods have been supported by theoretical and clinical evidence. In addition, therapeutic and theoretical evidences suggest that these three psychotherapies could be applied to different groups of depressed patients (53). On one hand, both CBT and IPT follow structured procedures with limited numbers of therapy sessions. However, CBT deals with the association between negative emotions and thoughts, while IPT deals with the association between negative emotions and corresponding life-events (mostly, interpersonal). On the other hand, psychodynamic psychotherapy deals with transference relationships, and its treatment principles are based on earlier theories of psychotherapy. Psychodynamic approaches have been claimed by a number of psychotherapists to be effective, but the classical psychoanalytic treatment is not suitable in the management of depression because the treatment is ultimately aimed at self-understanding and personality change. Especially, SPSP is defined as 16-session psychotherapy which focus on the affective, behavioral, and cognitive aspects of interpersonal or intrapersonal relationships (54). As a short term psychodynamic psychotherapy, SPSP recognizes the therapeutic utility of the transference relationship but does not interpret this relationship to the patient. Thus, among a number of self-care or psychotherapeutic methods, the Development Group regarded exercise therapy and bibliotherapy as self-care procedures available for mild or moderate depression, and also considered CBT, SPSP and IPT as available psychotherapeutic methods (8). Hence, our key questions referred to exercise therapy, bibliotherapy, CBT, SPSP, and IPT.

These key questions were designed to elicit accurate and correct answer, usually by employing the "PICO" method. The basic elements of a key question were P, I, C, and O, where P represents patients or the corresponding problems (patient population), I represents an intervention such as diagnostic evaluation, prognostic factors, and treatments (interventions), C represents an alternative intervention with which the former is to be compared (comparison), and O represents clinical outcome (outcome) (55).

Scope and process of literature search

Within the scope expressed in the Core Standard Ideal (COSI), the following literature sources were searched: PubMed, EMBASE, Cochrane CENTRAL, Korea Med, KMbase, RICH, and the National Assembly Library. Since systematic reviews and meta-analyses did not include Korean publications, the administrative researchers were obliged to search the literature manually and extract the contents of the relevant journals to access and evaluate original publications.

Literature search was carried out in several steps, including the development of the search strategy itself. First, the researcher who was responsible for selection of key questions converted the questions into the PICO format (55) and forwarded them to the literature search team. The team extracted preliminary search words and sent them back to the researcher in charge. Second, the team searched the database using the selected search words, listed the initial basic search results and abstracts, and sent this data back to the researcher in charge. Then, the researcher read and judged each abstract and created a list of suitable studies, given the key question being asked. The literature search team obtained the original publications in the list. Third, the researcher in charge received the original publications from the search team, read them carefully, and selected the publications to be used in the systematic review. Finally, the search team searched for published findings of randomized controlled trials (RCTs) conducted after the publication of the most recently selected systematic reviews.

Literature quality and evidence levels

For evaluation of each study, the Development Group used the Scottish Intercollegiate Guidelines Network (SIGN) grading system (56). Meta-analyses and RCT were allocated as top level

Table 1. Evidence levels for the 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea' (57)

Levels	Contents
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies High quality case controls or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

RCTs, Randomized Controlled Trials.

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evidence; un-randomized clinical research and observational research as mid level evidence; and, expert opinion and case reports were allocated as low level evidence. The SIGN systematic review evaluation method was generally used to judge the following criteria: first, if the research questions were carefully chosen and well-focused; second, if there was a methodologi-

Table 2. Recommendation grades for the 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea' (57)

Grades	Contents
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
Good Practice Point (GPP)	Recommended best practice based on the clinical experience of the guideline development group

Table 3. Evidence of the efficacy of exercise therapy for depression

Randomized controlled trials								
Authors, Year (Reference number)	Evidence level	Sample size	Characteristics of participants	Intervention	Comparison condition	Follow-up period	Outcome measures	Results (Effect size)
Babyak et al., 2000 (10)	1+	83	MDD adults	Exercise	Medication, Combination	10 months	HRSD, BDI	Six months after conclusion of the treatment program BDI scores did not differ between groups.
Blumenthal et al., 2007 (11)	1++	102	Major depression adults	Home-based exercise, Supervised exercise	Antidepressant (sertraline, 50-200 mg daily), Placebo	4 months	HRSD	The efficacy of exercise in patients seems generally comparable with antidepressant medication, and both tend to be better than the placebo.
Cramer et al., 1991 (12)	1-	35	Mildly obese women	Exercise	No exercise	15 weeks	POMS	Profiles of Mood State scores were not significantly related to exercise training.
Dunn et al., 2005 (13)	1+	31	Adults with mild to moderate depression	High-intensity aerobic exercise (17.5 kcal/kg/week)	Flexibility exercise (3 days/week)	12 weeks	HRSD	Aerobic exercise at a dose consistent with public health recommendations was an effective treatment for MDD of mild to moderate severity. A lower dose was comparable to placebo.
Greist et al., 1979 (14)	1-	28	Depressed adults	Running treatment	Time-limited psychotherapy, Time-unlimited psychotherapy	12 months	SCL-90	Running was as effective in reducing symptoms as either psychotherapy.
Krogh et al., 2009 (15)	1-	165	Adults with mild to moderate depression	Aerobic training (twice a week for 4 months), Strength training (twice a week for 4 months)	Relaxation training (twice per a week for 4 months)	4 months, 12 months	HRSD	No statistically significant effect of exercise on symptom severity in depressed patients.
Legrand et al., 2007 (16)	1-	15	Adults with mild to moderate depression	High-frequency aerobic exercise (3-5 times/week)	Low-frequency exercise (mainly, stretching)	8 weeks	BDI	Those in the high-frequency aerobic exercise group yielded lower depression scores than those in the low-frequency (control) group.
McCann et al., 1984 (17)	1-	47	Female college students with at least mild depression	Aerobic exercise	Relaxation exercise, Placebo	10 weeks	BDI	Subjects in the aerobic exercise condition benefited from reliably greater decreases in depression than subjects in the placebo condition or the non-treatment condition.
Nabkasorn et al., 2006 (18)	1-	49	Adults with mild to moderate depression	Exercise	Daily activity	16 weeks	CES-D	After the sessions of exercise the CES-D total depressive score decreased significantly, whereas no effect was observed after periods of normal daily activities.
Singh et al., 2001 (19)	1+	29	Depressed patients	Exercise under supervision (10 weeks) + subsequent individual exercise (10 weeks)	Supervision (10 weeks)	20 weeks, 26 months	BDI	BDI was significantly lower at both 20 weeks and 26 months of follow-up in exercisers compared with controls.

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cal description; third, if the literature search was comprehensive enough to discover all the appropriate findings; and fourth, if all the research findings were homogeneous enough to be combined together. Publications in languages other than Korean or English were excluded from the scope of this search. The Development Group had been trained by an expert of evidence-based medicine in evaluating the appropriate literature with experts in methodology, and such efforts were continued to unify the evaluation criteria used by all researchers.

Evidence levels used are summarized in Table 1 (57). These were prepared by systematically summarizing relative research findings to allow readers to compare the results in a single view. In general, the tables included research type and quality, research type, arbitration, confidence intervals, and results.

Recommendation grades

The Development Group classified grades of recommendation into 4 levels, A, B, C, and Good Practice Point (GPP), as indicated in Table 2. GPP is a recommendation grade with an evidence level of 3 or 4 (57). The development of recommendations consisted of synthesizing and analyzing all the data gathered for each key question. However, if findings were diverse or controversial on a certain issue, the evidence was not consistent, most of the claims underlying the evidence were inadequate or poor, or if the evidence had a high evidence level but were of a lower clinical applicability, careful consideration were given to the recommendation grade. As a consequence, expert opinion sometimes influenced recommendation grades, and official agreement amongst all the researchers were used in place of evaluations from a single researcher.

External expert review and academy certification

The Development Group requested external experts to review the draft of the guideline for its feasibility and availability, and

Table 3. Continued

				Systemic review				
Authors, Year (Reference number)	Evidence level	Number of literature	Characteristics of participants	Intervention	Comparison condition	Searching database	Outcome measures	Results (Effect size)
Dunn et al., 2001 (20)	1+	16	Depression	Various intensity exercises Aerobic and resistance exercise	Light vs moderate vs vigorous exercise, Aerobic exercise vs resistance exercise	PubMed, Psychlit	BDI	All evidence for dose-response effects of physical activity and exercise is from B and C levels of evidence. There is evidence that both resistance and aerobic exercise can reduce symptoms of depression.
Ernst et al., 1998 (21)	1-	80	Depression	Exercise	Antidepressant, Psychotherapy		Meta-analysis	Exercise was as effective as antidepressant and psychotherapy. Overall mean exercise effect size of -0.53 (range, -3.88 to 2.05).
Lawlor et al., 2001 (22)	1++	14	Adults with depression	Exercise	No treatment, CBT	PubMed, EMBASE, Psychlit, Cochrane	BDI, Meta-analysis	Compared with no treatment, exercise reduced symptoms of depression; the effect size was -1.1 (range, -1.5 to -0.6). The effect of exercise was similar to that of cognitive therapy; the effect size was -0.3 (range, -0.7 to 0.1).
Mead et al., 2009 (23)	1++	28	Adults with depression	Exercise	Standard treatment, No treatment, Placebo treatment	PubMed, EMBASE, PsycINFO, Cochrane	Meta-analysis	Comparing exercise with no treatment or a control intervention, the effect size was -0.82 (range, 1.12 to -0.51), indicating a large clinical effect. The effect of exercise was not significantly different from that of cognitive therapy.
Morgan et al., 2008 (24)	1+	11	Adults with depression	Exercise	Waiting-list, Placebo, Low-intensity exercise, Health education	PubMed, PsycINFO, Cochrane	Meta-analysis	Compared to a control condition, meta-analysis found that exercise had a large effect, with effect size 1.42 (range, 0.92 to 1.93).
Rethorst et al., 2009 (25)	1+	58	Depression	Exercise	No treatment, Wait-list	PubMed, PsycINFO, SportDiscus	Meta-analysis	Compared with a control intervention, exercise led to significantly lower depression scores; overall effect size was -0.80.
Teychenne et al., 2008 (26)	1+	67	Adults with depression	Physical activity	Dose of physical activity (frequency, intensity and duration)	PubMed, PsycINFO, Science Direct	Meta-analysis	Both shorter and longer durations of PA were effective in reducing the likelihood of depression. Evidence suggests that even low doses of PA may protect against depression.

BDI, Beck Depression Inventory; CBT, cognitive behavioral therapy; CES-D, Center for Epidemiological Studies Depression Scale; HRSD, Hamilton Rating Scale for Depression; POMS, Profiles of Mood State; SCL-90, Symptom Checklist-90.

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the review result was considered for during the revision process after a subsequent internal discussion. The 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea' was certified at the Annual Meeting of the Korean Neuropsychiatric Association in April, 2010.

RESULTS

Key question 1. Is exercise therapy more efficacious than placebo or antidepressant for adult patients with mild or moderate depression?

Evidence: The evidence for efficacy of exercise therapy is presented in Table 3. Exercise therapy is more efficacious than no treatment for adult patients with mild-to-moderate depression, and its efficacy is similar to that of antidepressant treatment or cognitive behavioral therapy alone (Evidence Level: 1++).

Recommendations: Exercise therapy is recommended for adult patients with mild or moderate depression (Recommendation Grade: A). ***Structured*** exercise therapy may be considered a non-pharmacological treatment in adult patients with mild or moderate depression (Recommendation Grade: B).

Key question 2. Is bibliotherapy more efficacious than placebo or antidepressant for adult patients with mild or moderate depression?

Evidence: The evidence for efficacy of bibliotherapy is presented in Table 4. Bibliotherapy decreased the severity of depressive symptoms significantly, and the efficacy was reported to last for up to 6 months (Evidence Level: 1+).

Recommendations: Bibliotherapy may be considered a non-pharmacological treatment for adult patients with mild-to-moderate depression (Recommendation Grade: B).

Key question 3. Is cognitive-behavioral therapy (CBT) more efficacious than placebo and antidepressant treatment for adult patients with mild or moderate depression?

Evidence: The evidence for efficacy of CBT is presented in Table 5. CBT was considered to be more efficacious than placebo for adult patients with mild or moderate depression and to be as efficacious as antidepressant treatment alone (Evidence Level: 1+).

Recommendations: CBT may be considered a non-pharmacological treatment for adult patients with mild-to-moderate depres-

Table 4. Evidence of the efficacy of bibliotherapy for depression

Randomized controlled trials								
Authors, Year (Reference number)	Evidence level	Sample size	Characteristics of participants	Intervention	Comparison condition	Follow-up period	Outcome measures	Results (Effect size)
Wollersheim et al., 1991 (27)	1++	32	Depressed outpatients (22-68 yr)	Coping (n = 8), Supportive PT (n = 8), Bibliotherapy (n = 8)	Delayed treatment (n = 8)	6 months	BDI, MMPI (D)	All the interventions were effective.
Bowman et al., 1995 (28)	1++	30	Community-dwelling individuals (>18 yr), at least mild depression	Cognitive bibliotherapy (n = 10), Self-examination therapy (n = 10)	Waiting-list control group (n = 10)	2 months	HRSD, BDI, ATQ	All the interventions were effective.
Jamison et al., 1995 (29)	1+	80	Depressed adults from the community (18-60 yr)	Minimal-contact cognitive bibliotherapy (n = 40)	Waiting-list control group (n = 40)	3 months	HRSD, BDI, SCL-90	All the interventions were effective.
Mead et al., 2005 (30)	1+/-	114	Significant anxiety or depressive symptoms	Guided self-help (n = 57)	Routine care from primary-care professionals (n = 57)	3 months	HADS, BDI	No significant difference.
Systemic review								
Authors, Year (Reference number)	Evidence level	Number of literature	Characteristics of participants	Intervention	Comparison condition	Searching database	Outcome measures	Results (Effect size)
Anderson et al., 2005 (31)	1++	11	Aged over 16 yr, depression	Bibliotherapy	Usual treatment or waiting list comparison	PubMed, CINAHL, EMBASE, PsycINFO, CCTR, PsiTri	HRSD	Weak evidence of efficacy.
Fanner et al., 2008 (32)	1+	22	Depression + others	Bibliotherapy	Waiting list control group	PsycINFO, PubMed, LISA, EMBASE, CINAHL, King's Fund, Cochrane library, AMED	BDI, HRSD	Effective in the treatment of depression.
McNaughton, 2009 (33)	1+	9	Depression	Bibliotherapy, Computerized (or web-based) CBT	Various	PubMed, EMBASE, EBM Reviews		Bibliotherapy may be effective at primary care level.

ATQ, Automatic Thought Questionnaire; BDI, Beck Depression Inventory; CBT, cognitive behavioral therapy; HADS, Hospital Anxiety & Depression Scale; HRSD, Hamilton Rating Scale for Depression; MMPI (D), Minnesota Multiphasic Personality Inventory - Depression Scale; SCL-90, Symptom Checklist-90.

Table 5. Evidence of the efficacy of cognitive behavioral therapy for depression

Randomized controlled trials								
Authors, Year (Reference number)	Evidence level	Sample size	Characteristics of participants	Intervention	Comparison condition	Follow-up period	Outcome measures	Results (Effect size)
Wong, 2008 (34)	1-	96	MDD	CBT	CBT vs waiting-list control	10 weeks	BDI Q-LES	CBT was superior to waiting list ($P < 0.001$).
Wong, 2008 (35)	1-	347	MDD	CBT	CBT vs waiting-list control	10 weeks	BDI	CBT was superior to waiting.
Dimidjian et al., 2006 (36)	1+	241	MDD	CBT, AD (paroxetine), BA	CBT vs paroxetine vs BA vs placebo	8 weeks	HRSD BDI	No significant difference among CBT, AD, BA, and placebo in less severe depression.
Ward et al., 2000 (37)	1-	75	MDD	CBT, AD (fluoxetine, bupropion)	CBT (n = 52) vs AD (n = 10: fluoxetine, n = 13: bupropion)	16 weeks	HRSD BDI	AD was superior to CBT (BDI: $P = 0.008$, GAS: $P = 0.005$).
Elkin et al., 1989 (38)	1+	240	MDD	Imipramine, CBT, IPT	CBT IPT Imipramine+clinical management Placebo+clinical management	16 weeks	HRSD BDI SCL-90	No significant differences found among imipramine, CBT, and IPT in mild depression.
Systemic review								
Authors, Year (Reference number)	Evidence level	Number of literature	Characteristics of participants	Intervention	Comparison condition	Searching database	Outcome measures	Results (Effect size)
Gloaguen et al.,1997 (39)	1-	48	MDD, Dysthymia (mild to moderate)	CBT, BT, AD, Placebo, Wait-list	CBT vs waitlist or placebo CBT vs AD CBT vs BT CBT vs other therapies	EMBASE PubMed	BDI	CBT was more effective than AD ($P < 0.001$).
Parker et al., 2008 (40)	1-	9	MDD, Dysthymia (mild to moderate)	CBT, AD	CBT vs AD	EMBASE PubMed	BDI	Little difference in efficacy was found between CBT and AD.

AD, Antidepressant; BA, Behavioral Activation; BDI, Beck Depression Inventory; BT, Behavioral Therapy; CBT, Cognitive Behavioral Therapy; HRSD, Hamilton Rating Scale for Depression; IPT, Interpersonal Psychotherapy; Q-LES, Quality of Life Enjoyment and Satisfaction; MDD, major depressive disorder; SCL-90, Symptom Checklist-90.

sion (Recommendation Grade: B).

Key question 4. Is CBT more efficacious than other psychotherapies for adult patients with mild or moderate depression?

Evidence: The evidence for efficacy of CBT is shown in Table 5. The efficacy of CBT appears similar to that of other interpersonal psychotherapies or other kinds of psychotherapy (Evidence level: 1+).

Recommendations: CBT may be considered a non-pharmacological treatment in adult patients with mild-to-moderate depression (Recommendation Grade: B).

Key question 5. Is short-term psychodynamic supportive psychotherapy (SPSP) more efficacious for adult patients with mild or moderate depression than placebo or antidepressant?

Evidence: The evidence for efficacy of SPSP is shown in Table 6. SPSP is expected to have a similar efficacy to pharmacological treatment alone for mild or moderate depression. In particular, combination SPSP-pharmacological therapy may be considered not only for improving depressive symptoms but also for improving social function and reducing the rate of discontinuation of treatment (Evidence Level: 1+).

Recommendations: SPSP may be considered a non-pharmacological treatment in adult patients with mild-to-moderate depression (Recommendation Grade: B).

Key question 6. Is interpersonal psychotherapy (IPT) more efficacious for adult patients with mild or moderate depression than placebo or antidepressant?

Evidence: The evidence for efficacy of IPT is shown in Table 7. IPT appeared to be more efficacious than placebo and at least as efficacious as pharmacological treatment alone for adult patients with mild or moderate depression (Evidence Level: 1+).

Recommendations: IPT may be considered a non-pharmacological treatment in adult patients with mild or moderate depression (Recommendation Grade: B).

Key question 7. Is combination IPT-pharmacological treatment more efficacious for adult patients with mild or moderate depression than single treatment (IPT or pharmacological treatment alone)?

Evidence: The evidence for efficacy of IPT is given in Table 7. In

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Table 6. Evidence of the efficacy of short-term psychodynamic supportive psychotherapy for depression

Randomized controlled trials								
Authors, Year (Reference number)	Evidence level	Sample size	Characteristics of participants	Intervention	Comparison condition	Follow-up period	Outcome measures	Results (Effect size)
de Jonghe et al., 2004 (41)	1+	208	Mild to moderate depression	SPSP	SPSP+pharmacotherapy	6 months	HDRS, CGI-S	Both SPSP & CoT were effective in reducing symptoms. Advantages of both treatments appeared to be equivocal.
de Jonghe et al., 2001 (42)	1+	167	MDD adults	SPSP+ pharmacotherapy	Pharmacotherapy	6 months	HDRS, CGI-S, QLDS	CoT led to significantly less rates of drop-out & more rates of recovery than pharmacotherapy.
Dekker et al., 2008 (43)	1+	141	Adults with depressive episode	SPSP	Pharmacotherapy	8 weeks	HDRS	Pharmacotherapy was more effective than SPSP in the first 8 weeks of treatment.
Dekker et al., 2005 (44)	1+	103	MDD adults	8-session SPSP	16-session SPSP	24 weeks	HDRS, CGI-S, QLDS	Equally effective.
Kool et al., 2003 (45)	1+	128	MDD adults with personality disorder	SPSP+ pharmacotherapy	Pharmacotherapy	6 months	HDRS	CoT was more effective than pharmacotherapy for depressed patients with personality disorder.
Molenaar et al., 2007 (46)	1+	167	MDD adults	SPSP+ pharmacotherapy	Pharmacotherapy	6 months	HDRS, CGI-S, QLDS, GSDS	Moderate advantage of CoT over pharmacotherapy.
Systemic review								
Authors, Year (Reference number)	Evidence level	Number of literature	Characteristics of participants	Intervention	Comparison condition	Searching database	Outcome measures	Results (Effect size)
de Maat et al., 2008 (47)	1-	3	Mild to moderate depression	SPSP	Pharmacotherapy SPSP+pharmacotherapy	N/A	HDRS, CGI-S, QLDS	CoT was more effective than pharmacotherapy. SPSP & pharmacotherapy seemed to be equally effective.

CGI-S, Clinical Global Impression of Severity; CoT, Combined therapy; HDRS, Hamilton Depression Rating Scale; GSDS, Groningen Social Disability Schedule; SPSP, Short-term Psychodynamic Supportive Psychotherapy; QLDS, Quality of Life Depression Scale.

adult patients with mild or moderate depression, the efficacy of combination of IPT and pharmacological treatment is not significantly greater than that of pharmacological treatment alone, but the combination treatment been suggested to be more efficacious than pharmacological treatment alone for severe depression (Evidence Level: 1+).

Recommendations: The combination of IPT and pharmacological treatment does not seem to be more efficacious than pharmacological treatment alone for mild or moderate depression, but the combination treatment may be considered for severe depression (Recommendation Grade: B).

DISCUSSION

The present guideline was developed to improve the quality of treatment and reduce the differences in clinical practice, inappropriate treatment and treatment cost in the management of Korean adults with mild-to-moderate depression. In addition, evidence-based findings on medical cost, outcomes, and patient preferences have been incorporated in the guideline to support the medical decision-making process. Presently, evidence-based treatment guidelines have been developed in the USA, UK, Canada, New Zealand, and Singapore (3, 4). There are two main reasons why these standardized guidelines have been developed. First, no one individual can keep up with the rate of development of medical knowledge given the increasing number of studies published. Second, expert recommendations often contradict each other, and advice regarding clinical treatment can vary significantly depending on the source of a given knowledge. In Korea, very little high-quality RCTs on the management of depression and the absence of an internet-based domestic literature database have hindered access to what little evidence-based knowledge is available for the treatment of depression.

There are a considerable number of treatments whose efficacy has been verified in favorable clinical trials, and the two most representative of these treatments are pharmacological therapy (mainly, antidepressant) and CBT. However, patients with depression prefer self-care and alternative therapies before seeking either of these two treatments (58), and this is particularly true in Korea (8, 53). In the initial phase of depression, a patient may find self-care desirable, when considering problems of cost, geographical hindrance, time, or the stigma associated with seeking professional psychiatric care. Thus, depression self-care treatments should be considered for the advantages of cost, prevention of adverse effects of pharmacologic therapy, and con-

Table 7. Evidence of the efficacy of interpersonal psychotherapy for depression

Randomized controlled trials								
Authors, Year (Reference number)	Evidence level	Sample size	Characteristics of participants	Intervention	Comparison condition	Follow-up period	Outcome measures	Results (Effect size)
Dimascio et al., 1979 (48)	1-	150	Neurotic depression (DSM-II)	Amitriptyline, IPT	Amitriptyline+IPT, Placebo+IPT, No pill+IPT, Amitriptyline+low interpersonal contact (LIC), Placebo+LIC, No pill+LIC	32 weeks	HSC, HRSD, SAS	There was no significant difference between pharmacotherapy alone and combination therapy (IPT+ pharmacotherapy) ($P = 0.05$). Psychotherapy was effective in patients with problems of social adaptation and interpersonal relationships.
Weissman et al., 1979 (49)	1-	96	MDD	Amitriptyline	Amitriptyline+IPT, Amitriptyline alone, IPT alone, Usual care	16 weeks	RDS, HRSD	Psychotherapy was similar to pharmacotherapy in terms of effect ($P < 0.05$, $P < 0.001$). Low recurrence rate of combination therapy (psychotherapy+ pharmacotherapy) as compared with pharmacotherapy alone ($P < 0.10$)
Elkin et al., 1989 (38)	1+	240	MDD	Imipramine, CBT, IPT	CBT, IPT, Imipramine, Placebo	16 weeks	HRSD, BDI, SCL-90	Effective in severely depressed patients who received IPT alone and medication alone ($P = 0.049$).
Systemic review								
Authors, Year (Reference number)	Evidence level	Number of literature	Characteristics of participants	Intervention	Comparison condition	Searching database	Outcome measures	Results (Effect size)
de Mello et al., 2005 (50)	1+	13	Dysthymia, MDD (postpartum), Double depression, Major depression, Recurrent major depression, Mood disorder Neurotic depression (DSM-II)	IPT, Medication (moclobemide, sertraline, nortriptyline, imipramine, amitriptyline), Placebo, CBT	IPT alone vs medication, IPT+medication (combined therapy) vs medication alone, IPT vs placebo, IPT vs CBT	EMBASE, LILACS, PsycINFO, Cochrane Depression, Anxiety and Neurosis Group Database of Trials, Cochrane Controlled Trials Register, SCI-E	Various	IPT was superior to placebo ($P < 0.05$). There was no significant difference between combination therapy (IPT +pharmacotherapy) and pharmacotherapy alone. IPT was superior to CBT ($P < 0.05$).

BDI, Beck Depression Inventory; HDRS, Hamilton Depression Rating Scale; IPT, interpersonal psychotherapy; RDS, Raskin Depression Scale; SAS, Self-rating Anxiety Scale; SCL-90, Symptom Checklist-90.

tinuation of psychiatric treatment. Moreover, studies have been frequently reported specific patient groups which responded to these three psychotherapeutic methods (34-50). CBT has been reported to be most efficacious for depressed patients who suffer from anxiety symptoms but has preserved cognitive function. SPSP provides a 'support' aimed at satisfying the developmental needs which until the time of therapy had remained unfulfilled (59). SPSP can be described as being on the supportive side of the traditional 'supportive-expressive' line dividing the two main schools of psychoanalytic psychotherapies. IPT is considered efficacious for patients who are socially well adapted, with short-term psychodynamic psychotherapy reserved for patients with accompanying personality disorders (41, 60). Consequently, this guideline evaluated and reviewed the evidence regarding these three psychotherapies to allow tailored treatment of individual patients in their respective conditions.

A web-based survey for implementation of clinical practice guidelines for depression demonstrated that over half (55.7%) of 386 Korean psychiatrists had clinical experiences with the guide in practice. The obstacles to implement the guidelines for depression were regarded as lack of knowledge, difficulties in accessing the guidelines, lack of support for mental health services, and general attitudes toward guideline necessity. Moreover, adding a summary booklet, providing teaching sessions, and improving guidance delivery systems had been suggested as effective methods for increasing the depression treatment guideline usage (61). These findings can anticipate the limitations and usage increasing tools of the 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression.' The most significant limitation of the guideline was the poverty of evidence from lack of clinical studies within Korea. This was of utmost importance to secure such evidence from studies within Korea, because non-pharmacological treatment is greatly affected by social and cultural norms and practices (62). Moreover, there is no specific bibliotherapy tailored for depression. Likewise, no standardized protocol for SPSP exists, although a specific pro-

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tocol for IPT has recently been translated and introduced in Korea. Hence, it is important to develop or prepare a Korean-written specific book for bibliotherapy and a Korean version of specific protocol for SPSP. Despite these several limitations, the 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression' has the virtue of the first evidenced-based guideline of non-pharmacological treatments for Korean adults with mild or moderate depression.

CONCLUSIONS

The 'Evidence-Based, Non-Pharmacological Treatment Guideline for Depression in Korea' was developed through a comprehensive systemic review. It proposes that exercise therapy, bibliotherapy, CBT, SPSP, and IPT should be considered as valid non-pharmacological treatments for Korean adult patients with mild or moderate depression. Further development of a Korean-written specific book for bibliotherapy and a Korean version of specific protocol for SPSP is urgently needed in Korea.

DISCLOSURE

The authors have no conflicts of interest to disclose.

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