



# การรักษาผู้ป่วยโรคซึมเศร้าชนิด major depressive disorder ด้วย cognitive-behavioral therapy : การพัฒนาบุคลากรและประเมินการให้บริการในผู้ป่วยชาวไทย

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## บทคัดย่อ

ภูมิหลัง มีการศึกษาเกี่ยวกับประสิทธิผลของกระบวนการคิด-พฤติกรรมบำบัด (cognitive-behavioral therapy หรือ CBT) น้อยมากในประเทศไทย ผู้นิพนธ์เสนอที่จะพัฒนาหลักสูตรฝึกอบรมและประเมินประสิทธิผลและการยอมรับในผู้ป่วยโรคซึมเศร้าชาวไทยซึ่งไม่ตอบสนองต่อยาแก้ซึมเศร้า

วิธีการ ได้มีการจัดประชุมเชิงปฏิบัติการเรื่องการรักษาโรคซึมเศร้าด้วย CBT เป็นจำนวน 5 วัน โดยมีวิทยากรประกอบด้วยผู้เชี่ยวชาญระดับนานาชาติ 1 ท่านและผู้บำบัด (therapist) ชาวไทยที่ได้รับการรับรองอีก 2 ท่าน บุคลากรด้านสุขภาพจิต 10 คนเข้าร่วมการประชุมเชิงปฏิบัติการดังกล่าวและได้รับการคำแนะนำอย่างน้อย 8 ครั้งจากผู้บำบัดที่ได้รับการรับรองชาวไทย โดยอิงคู่มือการรักษาด้วย CBT สำหรับโรคซึมเศร้า 2-3 เล่ม ผู้ฝึกอบรมและผู้รับการอบรมชาวไทยได้ร่วมกันพัฒนาคู่มือการบำบัดรักษาฉบับภาษาไทยขึ้น ผู้บำบัดที่ได้รับการฝึกอบรม 4 คนเข้าร่วมกระบวนการประเมินการให้บริการโดยทำการรักษาผู้ป่วยโรคซึมเศร้าชนิด major depressive disorder จำนวน 15 รายซึ่งไม่ตอบสนองต่อการรักษาด้วยยาแก้ซึมเศร้านาน 4 สัปดาห์

ผลการศึกษา ผู้ป่วยชาย 3 รายและหญิง 12 รายเข้าร่วมงานวิจัย ก่อนได้รับการรักษาและเมื่อจบการรักษา ค่าเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) ของคะแนน Montgomery Asberg Depression Rating Scale (MADRS) เท่ากับ 33.4 (5.9) และ 7.9 (5.4) ตามลำดับ ( $p=0.000$ ) ค่าเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) ของคะแนน 9-item Patient Health Questionnaire (PHQ-9) เท่ากับ 28.3 (4.6) และ 14.5 (2.9) ตามลำดับ ( $p=0.000$ ) ผู้ป่วย 13 จาก 15 รายตอบสนองต่อการร่วมรักษาของยาแก้ซึมเศร้าและ CBT โดยเฉลี่ยแล้ว ผู้ป่วยพอใจการรักษาในครั้งแรกและพอใจมากเมื่อจบการรักษา

สรุป การรักษาด้วย CBT มีประโยชน์สำหรับผู้ป่วยโรคซึมเศร้ารุนแรงชาวไทยที่ไม่ตอบสนองต่อยาแก้ซึมเศร้า ผู้ป่วยส่วนใหญ่พอใจกับการรักษา ผลจากการศึกษานี้อาจนำไปขยายผลในการพัฒนาบุคลากรทางสุขภาพจิตในประเทศที่มีรายได้ต่ำและปานกลางได้ โดยนอกจากการฝึกอบรมเชิงปฏิบัติการแล้ว การประเมินการให้บริการก็เป็นสิ่งสำคัญ เพื่อให้มั่นใจว่าบริการใหม่ที่พัฒนาขึ้นมีคุณภาพและได้รับการยอมรับจากผู้ป่วย

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# Cognitive-behavioral Therapy for the Treatment of Major Depressive Disorder : Workforce Development and Service Evaluation in Thailand

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## Abstract

**Background:** Very few studies have been carried out to examine the efficacy of cognitive-behavioral therapy (CBT) in Thai depressed patients. The authors proposed to develop a training course and evaluate its efficacy and acceptability in Thai depressed patients not responding to antidepressants

**Methods:** An international expert and two Thai certified therapists held a 5-day workshop of CBT for depression. Ten mental health professionals attended the workshop and received at least 8 sessions of individual supervision from the Thai certified therapists. Based on a few handbooks of CBT for depression, Thai trainers and trainees jointly developed a treatment manual in Thai. Four trained therapists participated in service evaluation by treating 15 major depressed patients, who did not respond to 4-week treatment of antidepressants.

**Results:** Three male and 12 female patients participated in this study were treated by four newly trained therapists. At baseline and endpoint, mean scores (SDs) of the Montgomery Asberg Depression Rating Scale (MADRS) were 33.4 (5.9) and 7.9 (5.4), respectively ( $p=0.000$ ). Those of the 9-item Patient Health Questionnaire (PHQ-9) were 28.3 (4.6) and 14.5 (2.9), respectively ( $p=0.000$ ). Thirteen of 15 patients responded to the combined treatment of antidepressant and CBT. By average, patients were satisfied at the end of first treatment session and very satisfied at endpoint.

**Conclusions:** CBT is beneficial for Thai major depressed patients not responding to antidepressant therapy. Most patients are satisfied with the treatment. To develop workforce for providing psychosocial interventions in low- and middle-income countries, other steps additional to training workshops, in particular service evaluation, are necessary to ensure the quality of newly developed services and its worth for implementation.

**Key words:** cognitive-behavioral therapy, depressive disorder, Thai, workforce development, service evaluation

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## Background

Based on the cognitive model of emotional response, cognitive-behavioral therapy (CBT) is a form of psychotherapy that emphasizes the important role of thinking in how people feel and what people do. This time-limited psychotherapy (5-20 sessions) mainly focuses on here and now situations. Several lines of evidence have shown that CBT is an effective treatment for depression. Its efficacy is comparable to antidepressants in mild and moderate depressed patients<sup>1</sup>.

CBT is now a treatment of choice for depression in most contemporary treatment guidelines<sup>2-5</sup>. However, the evidence relevant to the application of CBT is rarely found in low and middle income countries. As depressed patients in low- and middle-income countries may have different perceptions, culture, values, and wishes on CBT, the evidence in this respect is relatively important. A Sri Lankan study of CBT for the reduction of medically unexplained symptoms, which are a frequent presentation of depression and anxiety, has found that CBT can reduce symptoms, visits, and distress, and increase patient satisfaction in the short term (3 months)<sup>6</sup>. A study in Nigeria has found that, to match with African patients' need, CBT should be modified, especially the smaller number of treatment sessions<sup>7</sup>.

Although CBT for depression has been implemented by many Thai psychiatrists and psychologists over the past several years, very few studies have been carried out to examine its efficacy in Thai depressed patients. In addition, the attitude of depressed patients towards the application of CBT has not yet known. The authors therefore proposed to investigate its efficacy and acceptability in Thai depressed

patients not responding to antidepressants, which is a common group of patients usually given CBT.

## Methods

We developed a training system for Thai mental health professionals and invited them to be trained therapists. After the finish of training, we carried out a 16-week, open-label study of the efficacy and acceptability of CBT in major depressed patients not responding to 4-week treatment of antidepressants. The study was approved by the ethics committee of each study sites. After the details of the study were fully explained, written informed consent was obtained from the patients before they participated in the study.

### *Therapists*

The study therapists were psychiatrists and psychiatric nurses, who had been working in university or mental health hospitals for many years. To ensure the quality of CBT given in this study, a qualified trainer from UK was invited to give a 5-day workshop of CBT to the study therapists. The study therapists had to practice CBT for treating depressed patients and received at least 8 supervision sessions from an author (NP) and another Thai qualified therapist. At the end of the training and supervision, NP and study therapists developed a Thai manual of CBT for depression which would be used by every therapist throughout the study.

### *Participants*

Depressed outpatients of participating hospitals were invited to join the study. The inclusion criteria were as follows: i) male or female; ii) aged between 18 and 60 years old; iii) meeting the DSM-IV diagnostic

criteria of major depressive disorder; iv) not response to four-week treatment of an approved antidepressant given at the recommended dose; and v) moderate or severe depression indicated by the Montgomery-Asberg Depression Rating Scale (MADRS) between 22 and 44 points<sup>8</sup>.

The exclusion criteria were: i) history of psychotic or bipolar disorder; ii) current diagnosis of substance dependence (except nicotine and caffeine); iii) moderate suicide behavior or higher indicated by the MADRS suicidal behavior item score of 4 or higher; iv) physical illness that may interfere the treatment or treatment response; and v) receiving formal psychotherapy during 3 months prior to the enrolment.

### Assessment and outcomes

Subjects were evaluated at baseline (week 0), week 4, week 8, week 12, and week 16 (or end of treatment) by the following measures:

1. Severity of depressive symptoms: MADRS; Clinical Global Impression - Severity (CGI-S)<sup>9</sup>, and 9-item Patient Health Questionnaire (PHQ-9)<sup>10</sup>
2. Quality of life: 26-item WHOQOL-BREF (Thai version)<sup>11</sup>
3. Patient satisfaction: 5-point scale, from 0 (not at all) to 4 (very satisfied).

### Interventions

In addition to the antidepressants given prior to the enrolment, CBT was given to all subjects. Thai manual-driven CBT was given weekly or biweekly (depend on subjects' convenience) at the maximum of 16 sessions. The antidepressant doses could not be increased during the study. The patients received

CBT with free of charge and could reimburse the transportation cost of 300 Thai Baht per visit. Every therapy session was digitally taped and randomly evaluated by an author (NP) to ensure the quality of therapy process. The records were destroyed at the end of the study.

### Statistical analysis

The data were analyzed on an intention-to-treat basis. The data of patients assessed at least once (at week 4) were included in the analysis. Response to treatment was defined by the 50% decrease of the MADRS scores. Remission was defined by the MADRS scores of 10 or less. Last observation carried forward analysis was applied for the MADRS, CGI-S, PHQ-9, WHOQOL-BREF, and satisfaction scores. Significant differences of the ordinal data were examined by using the Friedman's two way analysis of variance.

### Results

Three male and 12 female patients with a mean (SD) age of 34.3 (10.9) years old participated in this study. Six, eight, and one were single, married, and widow, respectively. Mean (SD) years of education was 12.7 (4.6) years. Mean (SD) ages at first diagnosis of depression and at first treatment for depression were 30.9 (11.3) and 31.1 (11.2) years old, respectively. Their antidepressants given for at least 4 weeks prior to the enrolment were as follows: i) fluoxetine 20 mg/day (11 patients); ii) fluoxetine 40 mg/day (2 patients); and iii) mirtazapine 30 mg/day (1 patient). One patient had a comorbidity of obsessive-avoidance personality trait. The numbers of patients returned at week 4, 8, 12, and 16 were 14, 11, 6, and 1, respectively. The data of

14 patients returned at week 4 were included in the analysis.

Of 14 patients, the numbers of patients responded to treatment and remitted at each point of time were as follows: 6 (42.9%) and 3 (21.4%) at week 4; 13 (92.9%) and 6 (42.9%) at week 8; 13 (92.9%) and 8 (57.1%) at week 12 and 16. Table 1 shows the significant differences of the MADRS, CGI-S, PHQ-9, WHOQOL-BREF, and patient satisfaction scores among five time points of assessment.

## Discussion

The addition of CBT improves the condition of major depressed patients not responding to four-week

antidepressant therapy. The reduction of MADRS and PHQ-9 scores suggests that both patient and therapist can observe the decrease of depressive symptoms. Patient global mental health and quality of life are also improved as measured by the CGI-S and WHOQOL-BREF. In addition, the patients are satisfied with the addition CBT.

The study results support the generalizability of CBT efficacy evidenced from western countries in Thai depressed patients<sup>12</sup>. The high discontinuation rate prior to week 12 (8/14 or 57.1%) in this Thai population is higher than that rate in a 10-week study carried out in Italy (3/19 or 15.8%)<sup>13</sup>. This high discontinuation rate may reflect a need for fewer CBT sessions, which has also been found in Nigeria patients<sup>7</sup>.

**Table 1** Treatment outcomes of major depressed patients receiving antidepressants plus CBT as measured by MADRS, PHQ-T, CGI-S, WHOQOL-BREF, and patient satisfaction<sup>a</sup>

Outcome measure	Mean (SD); N=14					Significant difference (Friedman's test)
	Week 0 (n=14)	Week 4 (n=14)	Week 8 (n=11)	Week 12 (n=6)	Week 16 (n=1)	
MADRS	33.4 (5.9)	17.3 (9.0)	12.3 (6.9)	8.2 (5.5)	7.9 (5.4)	$\chi^2=44.00$ , df=4, p=0.000
CGI-S	4.5 (1.0)	2.5 (1.1)	2.0 (0.9)	1.5 (0.8)	1.5 (0.8)	$\chi^2=40.32$ , df=4, p=0.000
PHQ-9	28.3 (4.6)	19.4 (5.8)	16.9 (4.6)	14.5 (2.9)	14.5 (2.9)	$\chi^2=35.56$ , df=4, p=0.000
WHO-QOL BREF, physical health	18.4 (3.6)	22.1 (3.4)	23.3 (3.8)	23.6 (3.6)	23.6 (3.6)	$\chi^2=36.15$ , df=4, p=0.000
WHO-QOL BREF, mental health	15.9 (3.0)	18.4 (3.2)	20.6 (4.2)	21.4 (3.4)	21.4 (3.4)	$\chi^2=32.49$ , df=4, p=0.000
WHO-QOL BREF, social relationship	7.4 (1.7)	9.7 (2.4)	10.6 (2.0)	11.4 (1.4)	11.4 (1.4)	$\chi^2=42.86$ , df=4, p=0.000
WHO-QOL BREF, environment	22.2 (5.2)	26.9 (4.7)	29.1 (4.7)	30.4 (4.3)	30.4 (4.3)	$\chi^2=32.04$ , df=4, p=0.000
Patient satisfaction	3.3 (0.6)	3.6 (0.5)	3.8 (0.4)	3.9 (0.3)	3.9 (0.3)	$\chi^2=22.94$ , df=4, p=0.000

<sup>a</sup>Last-observation-carried-forward analysis by including the data of 14 subjects evaluated at least once after receiving CBT

MADRS: Montgomery-Asberg Depression Rating Scale; PHQ9-T: 9-Item Patient Health Outcome; CGI-S: Clinical Global Impression - Severity; WHOQOL-BREF: World Health Organization Quality of life - BREF

Different from most CBT studies, the therapists in this study were newly trained. Their competence is therefore close to the real world one. This study may have two major limitations. First, the open study design may cause a bias. However, the agreement on self-administer and rating scales on decreased depressive symptoms may give some confidence on the results. Second, a large number of subjects dropped out during the study. Only one patient was the completer. Although the LOCF analysis has taken into account the data of subjects who lost to follow-up, the high drop-out rate would be more or less affect the results. Last, four-week antidepressant therapy might be too short to be sure that the patients were truly resistant to the given antidepressants. Although six-week duration may be considered as an adequate duration of antidepressant treatment, recent evidence has shown that most depressed patients are likely to respond to antidepressants within four-week time. In a study of 2,848 patients with major depressive disorder who were treated with 7 different antidepressants and placebo, the mean (SD) time to onset of improvement was 13 (1) days and to response was 19 (1) days.<sup>14</sup>.

Because all therapists in this study were mental health professionals in psychiatric and university hospitals, it is not yet known whether this therapy can be applied by other health professionals in primary and secondary health care settings.

Developing mental health workforce for providing psychosocial interventions in low- and middle-income countries is challenging. Other steps additional to training workshops are necessary to ensure the quality of newly developed services and its worth for implementation. Examples of those are

individual supervisions, treatment manuals in local language, and service evaluations. Despite of some limitations, the results of this study suggest that CBT, developed in western countries, is effective and applicable for Thai depressed patients not responding to antidepressant therapy. Although the patients well accept the treatment, they may prefer a short duration of treatment program.

## Conclusions

CBT is beneficial for Thai major depressed patient not responding to antidepressant therapy. Most patients are satisfied with the treatment. To develop workforce for providing psychosocial interventions in low- and middle-income countries, other steps additional to training workshops, in particular service evaluation, are necessary to ensure the quality of newly developed services and its worth for implementation.

## List of abbreviations

CBT = cognitive-behavioral therapy

MADRS = Montgomery-Asberg Depression Rating Scale

CGI-S = Clinical Global Impression - Severity

PHQ-9 = 9-item Patient Health Questionnaire

WHOQOL-BREF = World Health Organization

Quality of life - BREF

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

MS: participated in the design of the study,

developed the statistical analysis plan, performed the statistical analysis, and preparing the manuscript.

NP: participated in the design of the study, developed the statistical analysis plan, trained the study therapists, and preparing the manuscript.

PK: participated in the design of the study, developed the statistical analysis plan, and preparing the manuscript.

AC: participated in the design of the study, trained the study therapists, and preparing the manuscript.

All authors read and approved the final manuscript

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