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## ECONOMIC EVALUATION

## Cost-Effectiveness Analysis for Antidepressants and Cognitive Behavioral Therapy for Major Depression in Thailand

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## ABSTRACT

**Objective:** To determine the cost-effectiveness of fluoxetine and cognitive-behavioral therapy (CBT) for major depression in Thailand. **Methods:** A microsimulation model was developed to describe the variation in course of disease between individuals. Model inputs included Thai data on disease parameters and costs while impact measures were derived from a systematic review and meta-analysis of the international literature. Fluoxetine as the cheapest antidepressant drug in Thailand was analyzed for treatment of episodes plus a 6-month continuation phase and for maintenance treatment over 5 years of follow-up. CBT was analyzed for episodic treatment and for 5-year maintenance treatment. Results are presented as cost (Thai bahts) per disability-adjusted life-year (DALY) averted, compared with a “do-nothing” scenario. **Results:** The cost-effectiveness ratios of all interventions were below 1 time Thailand’s gross domestic product of 110,000 bahts per capita. The uncertainty ranges

around the cost-effectiveness ratios overlap: maintenance treatment with CBT 11,000 bahts per DALY (8,000–14,000); episodic treatment with CBT 23,000 bahts per DALY (10,000–36,000); episodic plus continuation drug treatment 33,000 bahts per DALY (26,000–44,000); maintenance drug treatment 38,000 bahts per DALY (30,000–48,000); and episodic drug treatment 42,000 bahts per DALY (32,000–57,000). **Conclusions:** CBT and generic fluoxetine are cost-effective treatment options for both episodic and maintenance treatment of major depression in Thailand. Maintenance treatment has the greatest potential of health gain.

**Keywords:** health economics, major depressive disorder, pharmacotherapy, psychotherapy.

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### Introduction

Major depression has a large health and economic impact on individuals and communities. Up to 15% of patients with depression die from suicide over their lifetime [1]. By the year 2020, if the current demographic trends and epidemiological transition continue, the burden of depression will increase to 5.7% of the global burden of disease, becoming the second leading cause of disability-adjusted life-years (DALYs) lost, eclipsed only by ischemic heart disease in both males and females [2]. According to the Thai Mental Health Survey 2003, major depression was the most prevalent mental disorder in Thailand (3.2%; 95% confidence interval [CI] 2.9–3.5) [3]. Depressive disorder also imposes a significant burden in Thailand. It ranked as one of the top 10 causes of DALYs lost in Thailand in 1999, coming first for females and fourth for males [4]. Depression is also a costly disease. The high costs are not only the direct treatment costs, but there is also a large contribution from indirect costs including absenteeism, loss of opportunity, and productivity [5].

Previous studies have found that there are a variety of treatment options for improving the quality of life and social function of patients who have major depression [6–8]. In addition, effective treatment can decrease the financial burden of illness by reducing the direct and indirect costs associated with depression [9]. Effective interventions include antidepressant drugs and various methods of psychotherapy. The first-line treatment for most people with depression today consists of antidepressant drug therapy, psychological interventions, or a combination of the two. Among the psychotherapeutic approaches, cognitive-behavioral therapy (CBT) is an intervention recommended by clinical practice guidelines for the treatment of depression [7,8]. In Thailand, these interventions are currently recommended by the clinical practice guidelines for the treatment of major depressive disorder of the Royal College of Psychiatry of Thailand and the Psychiatric Association of Thailand [10]. CBT, however, is currently only sporadically available in Thailand. In general, the country has very few people with any psychotherapeutic skills. There are a number of antidepressant drugs in Thailand. Only two of them have generic versions available, fluoxetine and sertraline.

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Despite there being a range of options for treating patients with depressive disorders, even in high-income countries only one-third of patients receive effective treatments [11,12]. Even recently, the health insurance schemes that covered all Thai people—6 million (9%) covered by the Civil Servant Medical Benefit Scheme, 10 million (16%) covered by the Social Health Insurance scheme, and the rest of the population (47 million) covered by the Universal Coverage scheme [13]—estimated that only 4% of psychiatric patients received treatment [14]. In Thailand, resources currently allocated to meet the needs of patients with mental disorder are scarce [15]. Given finite resources in mental health personnel and budget, economic evaluation can help to determine the most cost-effective interventions among numerous intervention options available. Such evidence can help policy decision makers set priorities in terms of budget allocation [16].

Two articles have reviewed the effectiveness of CBT by newly trained Thai CBT therapists in Thai depressive patients [17,18]. Both were outcomes of a project to train mental health professionals in the treatment of major depression by CBT. In the first phase, 10 experienced mental health professionals were trained in a 5-day workshop by a qualified trainer from the United Kingdom. All trainees received at least eight sessions of supervision from two qualified Thai therapists. During the training, a Thai manual of CBT for depression was developed. In the last phase of the project, a 16-week, open-label study of the efficacy and acceptability of CBT in patients with major depression not responding to 4-weeks of treatment with fluoxetine was carried out.

The first study [18] reported outcomes in 15 patients treated by four newly trained therapists. Overall, the treatment program seemed effective in alleviating depression (13 of the 15 patients improved significantly), and patient satisfaction with treatment was high. Fifty-seven percent of patients, however, stopped treatment before week 12; only one completed all the 16 sessions. The authors concluded that CBT efficacy as evident in Western studies can be generalized to the Thai context. Nevertheless, the high discontinuation rate suggests that patients may prefer a shorter duration of treatment. The other study [17] reported that all 10 patients, of three newly trained therapists from this same CBT training program, responded by week 12 and 70% of them were in remission by week 12. Neither study had a control group and therefore provide insufficient evidence of effectiveness.

There is only one cost-effectiveness study of drug treatment of major depressive disorder in Thailand. It concluded that escitalopram was more cost-effective than fluoxetine and venlafaxine, but it did not consider the availability of a cheap generic version of fluoxetine [19]. There are no economic evaluations of psychotherapy in Thailand. Our study aims to inform policymakers of the most cost-effective intervention for major depression in Thailand.

## Methods

Cost-effectiveness analysis is a method of assessing the health consequences relative to the costs of different health interventions. It is used to identify health interventions that yield the highest benefit in health outcomes per monetary unit of health expenditure [20].

### Framing and design of the analysis

This study adopted a “health sector” perspective, arguing that it is most suitable to policymakers as part of decision making in health resource allocation. This perspective concerns the health-related costs borne by government and by individuals including time and travel costs. The comparator was a hypothetical “do-nothing” scenario-based on the generalized Cost-Effectiveness Analysis framework [21]. The target population in this study was those in

the Thai population in 2005 experiencing a major depressive episode. The time horizon for evaluating the benefits and costs of interventions for depression was over a 5-year follow-up period. This time horizon was considered appropriate for tracking the costs/cost offsets and consequences associated with the selected interventions as there was no information on the longer-term consequences of these interventions beyond 5 years. In addition, the natural history of depression can be reasonably described over a 5-year period, but there is a lack of data to accurately describe the course of major depression over a lifetime.

A 3% discount rate that matches the rate chosen in the Thai burden of disease study [4] was applied to both costs and benefits. It is also the rate of discounting recommended by a consensus panel of health economists in the United States [22], and it was in the range of 3% to 5% recommended by economic evaluation guidelines in Thailand [23].

### Description of interventions

Pharmacological interventions and CBT were selected for analysis by the steering committee and the expert advisory group for mental health in the Setting Priorities using Information on Cost-Effectiveness (SPICE) project, which was a collaborative project between the Ministry of Public Health, Thailand, and the University of Queensland, Australia. We undertook the current study as part of the SPICE project, which aimed to address key information gaps on burden of disease and cost-effectiveness across multiple disease areas in Thailand, with regard to policy concerns and technical rationality. The SPICE project included a cause of death study that aimed to improve the quality of cause of death statistics by deriving a “best” estimate of true cause-specific mortality in Thailand based on verbal autopsy interviews of 11,000 deaths and review of available medical records [24–27].

The interventions were classified by three phases of treatment: First, the acute or episodic phase is the time period from the initiation of treatment to remission (i.e., decrease in depressive symptoms to “normal”), which usually lasts between 8 and 12 weeks [12]. Second, the continuation phase is the period following the episodic phase for preventing relapse (i.e., the return to major depression). At least 6-months continuation therapy has been recommended by guidelines for the treatment of major depressive disorder [8,28]. Third, maintenance treatment may be given during a 5-year period following an episode to prevent recurrence (i.e., a new episode of major depression following recovery).

The drug interventions for major depression include the older tricyclic antidepressants, amitriptyline; the newer serotonin reuptake inhibitors, fluoxetine, sertraline, and escitalopram; and the newer serotonin norepinephrine reuptake inhibitor, venlafaxine. Generic serotonin reuptake inhibitors cost less than 10% of the cost of patented medications in Thailand. Meta-analyses show no difference in efficacy between antidepressant drugs [29,30]. Therefore, we analyzed generic fluoxetine only as the lowest cost antidepressant and the most commonly prescribed serotonin reuptake inhibitor in Thailand [31].

CBT is a nonpharmacological intervention that is effective in the treatment of depression alone or combined with drug therapy. A course of CBT during or following an acute episode has been found to prevent relapse for up to 1.5 years after an episode [32] and to further reduce recurrence if booster sessions are given as maintenance treatment [33,34]. CBT is a highly structured approach to psychotherapy with a shorter duration than most other therapies. The assumption of CBT is that emotional and behavioral problems are caused by cognitive or thought dysfunction. CBT is based on collaborative work between the therapist and the client. The therapist helps the client to identify emotions or feelings, negative automatic thoughts, and schema or core beliefs. This leads to modification of automatic thoughts and core beliefs in the end [35].

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