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# Cost-effectiveness analysis of aripiprazole compared with risperidone in the treatment of acute schizophrenia patients in Thailand

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## ABSTRACT

**Objectives:** Schizophrenia is the third leading cause of loss of life years in Thailand. Currently, aripiprazole is the latest drug for the treatment of acute schizophrenia in Thailand, but its cost-effectiveness has not been studied. The purpose of this study was to investigate the cost-effectiveness of aripiprazole compared with risperidone. **Methods:** A Markov model was used to evaluate total costs and quality-adjusted life years (QALYs) over a lifetime horizon from a societal perspective. Clinical effectiveness was retrieved from previous studies. All cost data and mortality rates were retrieved from Thai data. **Results:** The results revealed that the total cost of the treatment with aripiprazole was 691,469.06 Baht compared to 692,200.88 Baht for risperidone, and the QALYs were 15.75 and 15.45 years, respectively. The acceptability curves demonstrated that the probability of aripiprazole being cost-effective was 97.5% of the willingness-to-pay, being 1.2 times the Thai gross national income per capita. **Conclusions:** Treatment of acute schizophrenia in Thailand with aripiprazole was showed greater QALYs and lower cost than treatment with risperidone. Treatment with aripiprazole is a dominant alternative. The results of this study could contribute to appropriate decision-making by policymaker.

**Keywords:** Acute schizophrenia, aripiprazole, cost-effectiveness analysis, quality-adjusted life years, risperidone

## INTRODUCTION

Schizophrenia is a chronic psychiatric disorder that changes perception, thinking, and moods, and can have an effect on daily life, such as the ability to take care of oneself and live in society. Nowadays, schizophrenia is one of the 25 leading causes of disability worldwide.[1] The prevalence of schizophrenia in the Thai population is 8.8 per 1,000.[2] The annual overall cost of schizophrenia in Thailand is estimated to be THB 87,000 per person or THB 31,000 million nationally.[3]

The recommendations for antipsychotic drugs from the Psychiatric Association of Thailand 2013 contain no 1st line therapy for schizophrenia patients.[4] Atypical antipsychotics (the Second generation antipsychotics) are effective for both positive symptoms and negative symptoms with fewer extrapyramidal side effects (EPS) than conventional antipsychotics (typical antipsychotics). However, common adverse effects of atypical antipsychotics have been reported as metabolic adverse events, for example, weight gain, hyperlipidemia, and hyperglycemia.[5,6] Risperidone is the only one of atypical antipsychotics which on the National List of Essential Medicines (NLED) and reimbursable medicine. Despite being an effective and widely used in the treatment of schizophrenia in Thailand, it has been reported more EPS. This includes an increasing in serum prolactin levels, weight gain, and hyperglycemia.[7-9] Later, aripiprazole introduced as an effective atypical antipsychotic which has been approved by The United States Food and Drug Administration for the treatment of schizophrenia. It is more effective than other

atypical antipsychotics.[10] Besides, aripiprazole contributes to less EPS than other atypical antipsychotics. Furthermore, this latter treatment does not increase serum prolactin levels.[8-10]

Currently, risperidone is the only one of atypical antipsychotics on the NLED; therefore, it will be taken into account. Even though aripiprazole is more effective and causes fewer side effects than other antipsychotic drugs, the cost-effectiveness has not been reviewed.[11] Hence, the purpose of this study was to investigate the cost-effectiveness of aripiprazole compared with risperidone in the treatment of schizophrenia in Thailand.

## METHODOLOGY

### Study Design

This study was a health economic evaluation using a model-based structure and presented humanistic outcomes in quality-adjusted life years (QALYs). The analysis was assessed using incremental cost-effectiveness ratios. The perspective of this study was societal. Future costs and utilities were discounted at 3% per year.[12]

### Treatments

This study compared two antipsychotics medicines-aripiprazole and risperidone. The optimal dose for the treatment of schizophrenia patients is 15 mg per day of aripiprazole and 6 mg per day of risperidone.[13-15] Patients with schizophrenia who did not respond to aripiprazole or risperidone were switched to 300 mg per day of clozapine,[16] which is the only antipsychotics medicine that approved by FDA for treatment-resistant schizophrenia.[17]

### Decision Model

The model was developed based on previously published cost-effectiveness analyses of antipsychotics in schizophrenia.[5,18] A Markov model[19] was used to perform decision analysis by Microsoft Excel 2013. The model is presented in Figure 1 and was validated by three experts; one health economic expert validated the approach by validating the methodology, and two other clinical experts validated the sequence of the disease to ensure its appropriateness for schizophrenia treatment in Thailand. The base-case analysis was a hypothetical cohort of patients 15 years or older with stable schizophrenia who had no diabetes or hyperprolactinemia.

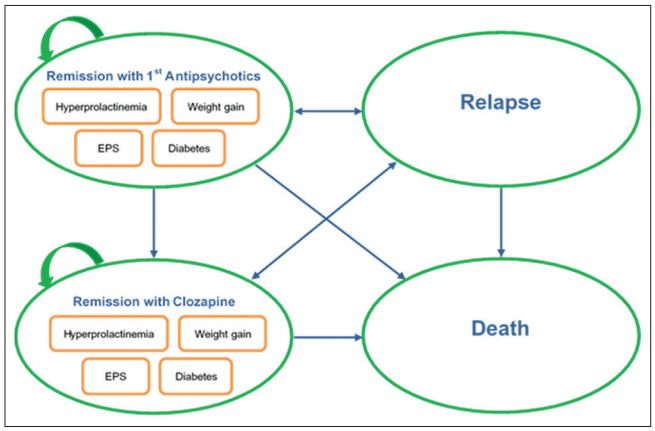


**Figure 1:** Markov model structure of Schizophrenia disease progression

### Assumptions of the Model

1. Patients did not drop out of any treatment during the study and remained until the end of the treatment.
2. All patients with aripiprazole or risperidone might experience common adverse drug reactions of atypical antipsychotics, being hyperprolactinemia, weight gain, diabetes or EPS, and other general adverse drug reactions.
3. Hyperprolactinemia was defined as a serum prolactin level ≥25 ng/mL and patients who experienced hyperprolactinemia were switched to clozapine.
4. Weight gain was defined as body weight increasing to ≥7% of basal body weight and patients who experienced weight gain were switched to clozapine.
5. Diabetes was defined as a plasma glucose level ≥200 mg/dl or fasting blood glucose (FBS) ≥126 mg/dl and could be reversible when treated with 1500 mg of metformin daily to controlled diabetes and patients who experienced diabetes were switched to clozapine.
6. EPS was assumed to be reversible when treated with 6 mg of trihexyphenidyl daily and patients who experienced EPS were switched to clozapine.
7. Patients with schizophrenia who did not respond to aripiprazole or risperidone, or who could not tolerate the adverse drug reactions involved were switched to clozapine until death.
8. Patients in a relapsed state of health were because of two conditions: (1) Non-compliance with, or inefficacy of aripiprazole or risperidone, or (2) Relapse from remission with taking clozapine.
9. Patients had not received other antipsychotics or other co-interventions.
10. The mortality rate of schizophrenia patients was determined by the age range equal to the mortality rate of the Thai population.[20]
11. Patients in all health states could be moved to the death state during the study period according to the normal mortality rate of the Thai population.

### Time Horizon

Almost every article showed the inclusion criteria of schizophrenia patients as 15–65 years old,[13,21] therefore a Markov model was developed to imitate the treatment of acute schizophrenia patients over a lifetime period from the age of 15 until death. The average life expectancy in Thailand was 74.9 years in 2015[22] which was used as a guideline for setting the time frame for this research study. A cycle length of 4 weeks was considered appropriate to capture both the clinical treatment and associated events such as relapses and adverse drug reactions from a survey of treatment in Thailand.[3]

### Probability of Clinical Outcomes

A search was conducted in Pubmed electronic and Cochrane databases. The key words were "Acute schizophrenia, Risperidone, Aripiprazole" with "And" and filtering by randomized controlled trial, meta-analysis, systematic reviews,

full text and English published literature. All searched literature was evaluated and given a Jadad score. All probabilities were converted into risks over 4 weeks because of the cycle length, and are shown in Table 1.

**Table 1:** All parameters used in the markov model

| Parameters | Distribution | Mean±SE | References |
|---|---|---|---|
| Probabilities | | | |
| Transition probabilities | | | |
| Aripiprazole | | | |
| Relapse | Beta | 0.0580±0.0015 | [5] |
| Inefficacy | Beta | 0.0408±0.0283 | [29] |
| Non-compliance | Beta | 0.0000±0.0000 | [21] |
| Intolerance to side effects | Beta | 0.0241±0.0169 | [21] |
| Risperidone | | | |
| Relapse | Beta | 0.0281±0.0004 | [5] |
| Inefficacy | Beta | 0.0000±0.0000 | [29] |
| Non-compliance | Beta | 0.0253±0.0177 | [21] |
| Intolerance to side effects | Beta | 0.0000±0.0000 | [21] |
| Clozapine | | | |
| Relapse | Beta | 0.0095±0.0021 | [30] |
| Probabilities of adverse drug reaction | | | |
| Aripiprazole | | | |
| Weight gain | Beta | 0.0161±0.0008 | [5] |
| Diabetes | Beta | 0.0016±0.0002 | [5] |
| EPS effects | Beta | 0.0056±0.0005 | [5] |
| Hyperprolactinemia | Beta | 0.0513±0.0353 | [29] |
| Risperidone | | | |
| Weight gain | Beta | 0.0189±0.0005 | [5] |
| Diabetes | Beta | 0.0023±0.0003 | [5] |
| EPS effects | Beta | 0.0089±0.0003 | [5] |
| Hyperprolactinemia | Beta | 0.9286±0.0487 | [29] |
| Costs (Baht) | | | |
| Medicine costs | | | |
| Aripiprazole 5 mg. (per tablet) (Originally made drug cost) | Gamma | 80.25±8.03 | [11] |
| Aripiprazole 15 mg. (per tablet) (Locally made drug cost) | Gamma | 80±8 | [11] |
| Risperidone 2 mg. (per tablet) (Originally made drug cost) | Gamma | 60.59±6.06 | [11] |
| Risperidone 2 mg. (per tablet) (Mean of locally made drug cost) | Gamma | 3.44±0.34 | [11] |
| Clozapine 100 mg. (per tablet) | Gamma | 1.91±0.19 | [11] |
| Trihexyphenidyl 2 mg. (per tablet) | Gamma | 0.20±0.02 | [11] |
| Metformin 500 mg. (per tablet) | Gamma | 0.32±0.03 | [11] |
| Laboratory costs | | | |
| FBS (per unit) | Gamma | 57.10±5.71 | [24] |
| HbA1c (per unit) | Gamma | 213.59±21.36 | [24] |
| Serum prolactin (per unit) | Gamma | 428.23±42.82 | [24] |
| CBC (per unit) | Gamma | 127.94±12.79 | [24] |
| Treatments and additional Procedures | | | |
| OPD service (per visit) | Gamma | 545.80±54.58 | [3] |
| Hospitalization (per admission) | Gamma | 23,590.45±2359.04 | [3] |

*(Contd...)*

**Table 1:** (*Continued*)

| Parameters | Distribution | Mean±SE | References |
|---|---|---|---|
| Psychoeducation (per year) | Gamma | 2,895.19±289.52 | [3] |
| Direct non-medical costs | | | |
| Travel (per visit) | Gamma | 238.15±23.82 | [3] |
| Family time (per year) | Gamma | 11,907.56±1190.76 | [3] |
| Meal (per visit) | Gamma | 68.33±6.83 | [24] |
| DW | | | |
| Remission state | Beta | 0.31±0.0264 | [25] |
| Utility weight | | | |
| Remission state | Beta | 0.69±0.0264 | [5] |
| Relapse state | Beta | 0.58±0.0282 | [5] |
| Weight gain | Beta | 0.66±0.0270 | [5] |
| Diabetes | Beta | 0.66±0.0270 | [5] |
| EPS effect | Beta | 0.62±0.0277 | [5] |
| Hyperprolactinemia | Beta | 0.62±0.0277 | [18] |

FBS: Fasting blood glucose, EPS: Extrapyramidal side effects, DW: Disability weights, HbA1c: HemoglobinA1c, CBC: Complete blood count

*Relapse*

In the base case, the 4 weeks rates of relapse were 5.8% for aripiprazole and 2.81% for risperidone.

*Hyperprolactinemia*

In the base case, the 4 weeks rates of relapse were 5.13% for aripiprazole and 92.86% for risperidone.

*EPS effect*

In the base case, the 4 weeks rates of relapse were 0.56% for aripiprazole and 0.89% for risperidone.

*Weight gain*

In the base case, the 4 weeks rates of relapse were 1.61% for aripiprazole and 1.89% for risperidone.

*Diabetes*

In the base case, the 4 weeks rates of relapse were 0.16% for aripiprazole and 0.23% for risperidone.

*Non-compliance*

In the base case, the 4 weeks rates of relapse were 0% for aripiprazole and 2.53% for risperidone.

*Inefficacy*

In the base case, the 4 weeks rates of relapse were 4.08% for aripiprazole and 0% for risperidone.

*Intolerance to side effects*

In the base case, the 4 weeks rates of relapse were 2.41% for aripiprazole and 0% for risperidone.

## Costs

All costs were expressed in Thai Baht and are shown in Table 1. Drug treatment costs were obtained from the Thai reference of drug costs from the Drug and Medical Supply Information Center, the Ministry of Public Health, Thailand,[11] and reports of local costs of aripiprazole by Srithanya hospital, Thailand.[23] Drug costs of risperidone 6 mg and aripiprazole 15 mg were obtained as mean of local version costs for base-case analysis and used original version costs for one-way sensitivity analysis, clozapine 300 mg, metformin 1,500 mg and trihexyphenidyl 6 mg were obtained as local version costs and calculated mean costs. All drug costs, costs of meals, and laboratory costs including tests for FBS, hemoglobinA1c, serum prolactin, and complete blood count were obtained from the mean cost per unit of secondary care by standard cost lists for health technology assessment in Thailand.[24] Costs of OPD services, hospitalization, psycho-education, travel expenses and family time were obtained from previous studies in Thailand. The frequencies of outpatient visits and admissions per year from surveys of mental illness in Thailand were 7.7 and 0.5, respectively.[3] All costs were adjusted to 2016 values using the consumer price index from the Bureau of Trade and Economic indices, The Ministry of Commerce, Thailand. Indirect costs were excluded from this study.

## Utility Values

The health outcomes were measured in utility weights for different health states and adverse drug reactions, ranging from 0 (death) to 1 (perfect health). Utility weights were multiplied by life-expectancies to generate QALYs.

Utility values of remission states were estimated based on the disability weights (DW) of remission states of Thai schizophrenia patients from a previous study[25] using the calculation, utility weight = 1 – DW.[26,27] Utility values of other health states were obtained from previous studies[5,18] and compared with the ratio of foreign utility weights and Thai utility weights to be converted into utility weights of Thai schizophrenia patients. All utility values are shown in Table 1.

## Sensitivity Analyses

A Monte Carlo Simulation was used for probabilistic sensitivity analyses by Microsoft Excel 2013. All variables were randomized 1,000 times by probability distribution and the ICER estimated. Beta distribution was used for transition probabilities and gamma distribution was used for costs. Net monetary benefit (NMB) was used to assess the cost-effectiveness in the probabilistic sensitivity analyses. The NMB calculation of aripiprazole compared with risperidone was formulated as follows:[28]

$$NMB = ([QALYs_{Aripiprazole} - QALYs_{Risperidone}] \times \text{Willingness to Pay[WTP]}) - (Costs_{Aripiprazole} - Costs_{Risperidone})$$

The results are shown as a cost-effectiveness plane between incremental costs and incremental QALYs, and a cost-effectiveness acceptability curve between probabilities of aripiprazole and risperidone and WTP. The results of one-way sensitivity analyses were shown in tornado diagram.

# RESULTS

## Cost-effectiveness Analysis

The results in Table 2 revealed that the total costs of the treatment with aripiprazole were 691,469.06 Baht compared to 692,200.88 Baht for risperidone, and the QALYs were 15.75 and 15.45 years, respectively. Treatment with aripiprazole showed lower cost than treatment with risperidone. The incremental QALY was 0.3 year. Treatment with aripiprazole is a dominant alternative because of greater QALYs and lower cost.

## Sensitivity Analyses

The probabilistic sensitivity analysis in Figure 2 presents the incremental costs and QALYs for aripiprazole compared with risperidone as a cost-effectiveness plane. After randomizing each variable 1,000 times in the Monte Carlo simulation, and evaluating the simultaneous uncertainties regarding each parameter which might influence the base-case ICER, an estimate of ICER is represented by the large point. The base-case ICER falls below the WTP line of 160,000 Baht. This revealed a probability of 97.5% that aripiprazole was cost-effective compared to risperidone.

The cost-effectiveness acceptability curve in Figure 3 shows a probability of 97.5% that aripiprazole was cost-effective compared to risperidone. If the WTP is increased, the probability that aripiprazole will be cost-effective compared to risperidone will increase.

The one-way sensitivity analysis in Figure 4 was presented in tornado diagram. The cost of original version of aripiprazole had the most impact on the ICER. The cost of original and generic version of aripiprazole was 240.75 baht per day and 80 baht per day, respectively. The cost of original and generic version of risperidone was 181.77 baht per day and 9.90 baht per day respectively. The discount rate varied from 0 to 6% per year.

# DISCUSSION

This analysis is the first economic evaluation to assess atypical antipsychotics, and to compare risperidone on the NLED,

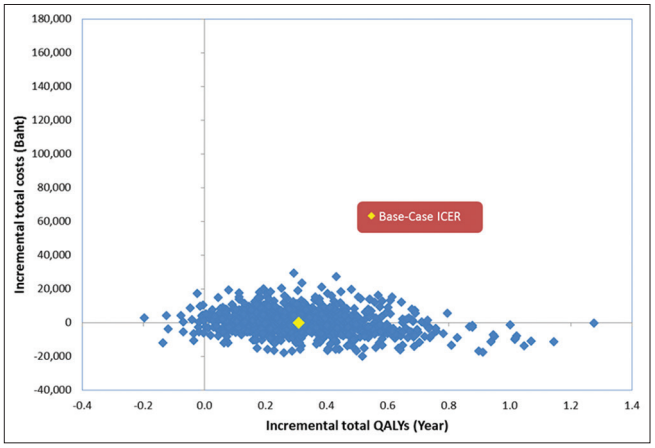


**Figure 2:** The cost-effectiveness plane between aripiprazole and risperidone

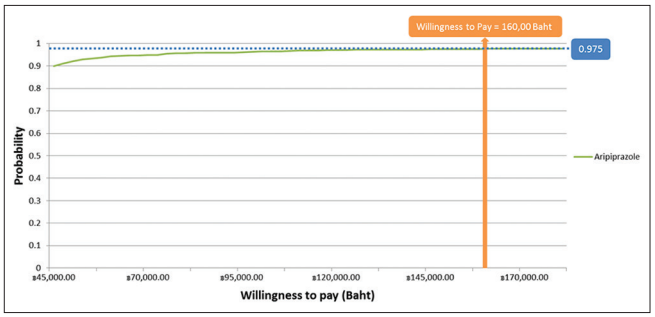


**Figure 3:** Cost-effectiveness acceptability curve

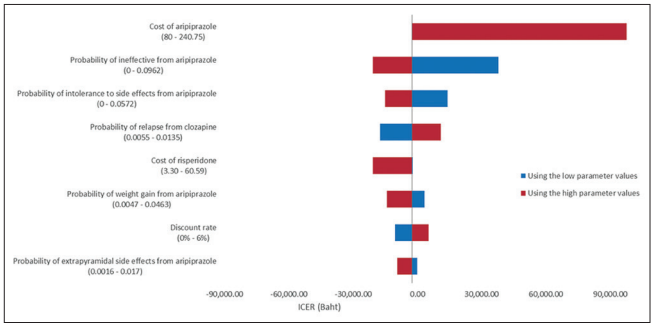


**Figure 4:** Tornado diagram showing the results of one-way sensitivity analysis

**Table 2:** Results

| Results | Total costs (Baht) | QALYs (Year) | Incremental costs (Baht) | Incremental QALYs (Year) | ICER (Baht/QALY gained) |
|---|---|---|---|---|---|
| Aripiprazole | 691,469.06 | 15.75 | | Dominant | |
| Risperidone | 692,200.88 | 15.45 | | | |

QALYs: Quality-adjusted life years

and aripiprazole, for the treatment of schizophrenia patients in Thailand. The results of this study found that aripiprazole was cost-effective when compared with risperidone in the treatment of patients with acute schizophrenia when considering a willingness-to-pay threshold of 160,000 Baht per QALY. Furthermore, aripiprazole produced better clinical outcomes in terms of QALYs than risperidone by 0.3 of a year. Moreover, aripiprazole involved lower expenditure and its ICER is below the GNI per capita and the selection criterion of 160,000 Baht per QALY. The cost-effectiveness criterion for drug selection in the Thailand National Primary Drug Register in the year 2013 currently used a WTP threshold of 160,000 Baht or 1.2 times of the Thai gross national income (GNI) per capita.[12]

In consequence, aripiprazole was cost-effective for the treatment of acute schizophrenia patients compared to risperidone. Corroborating the clinical results of earlier published studies showed that aripiprazole was more cost-effective than risperidone, olanzapine, and quetiapine for patients with schizophrenia treated in the community.[10] In contrast, a study from Singapore[5] found that olanzapine was the most cost-effective in relapse prevention when compared with 10 other atypical antipsychotics, including aripiprazole and risperidone. That result might be due to the healthcare perspective employed in that study, whereas this study adopted a societal perspective which was more extensive so that it could take into account the impact of the costs for analysis. Besides, the costs of olanzapine were similar to those of aripiprazole and higher than risperidone in Thailand. Moreover, hyperprolactinemia, which is an important adverse event which occurs with olanzapine more than aripiprazole, wasn't considered in that study. The cost of diagnosis of hyperprolactinemia is also high which could have an effect on these different results. One study reported that risperidone was responsible for a greater increase in serum prolactin than most other atypical antipsychotics.[31] This study also undertook analyses to determine the influence of these variables.

The costs were obtained from the Thai reference drug pricing. In this study also concerned a considerable difference in price between the original drug and the locally made drug. If the cost were set the baseline using a locally made drug price, it would omit the factors related to the original drug price. Therefore, the study adopted the mean of the price of original and locally made drug price to represent the drug cost in the sensitivity analysis. Hence, this allows the researchers to study and gained results from the condition that familiar to the real-life situation.

Several limitations exist in our study that should be acknowledged. First, regarding the probabilities of transitional health states, due to a lack of data about probabilities of transitional health states and adverse events from drug usage in Thailand, the data in this study were collected overall from foreign countries. Furthermore, the probabilities in this study were collected from acute relapse schizophrenia patients and from several studies by systematic search. Each study had definitions of the selected population in different states such as acute relapse schizophrenia patients, newly admitted patients, and stable patients. Second, regarding the humanistic outcome, several of the durations and disease health states used in this study to calculate the utility weight of health states and adverse drug reactions were compared with utility weights of foreign countries in remission state. The formulation was utility weight = 1 – DW.[26,27]

## CONCLUSIONS

Treatment of acute schizophrenia in Thailand with aripiprazole was showed greater QALYs and lower cost than treatment with risperidone. Treatment with aripiprazole is a dominant alternative. The results of this study could contribute to appropriate decision-making by policymaker.

## ACKNOWLEDGMENT

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## REFERENCES

1. Chong HY, Teoh SL, Wu DB, Kotirum S, Chiou CF, Chaiyakunapruk N. Global economic burden of schizophrenia: A systematic review. Neuropsychiatr Dis Treat 2016;12:357-73.
2. Phanthunane P, Vos T, Whiteford H, Bertram M, Udomratn P. Schizophrenia in Thailand: Prevalence and burden of disease. Popul Health Metr 2010;8:24.
3. Phanthunane P, Whiteford H, Vos T, Bertram M. Economic burden of schizophrenia: Empirical analyses from a survey in Thailand. J Ment Health Policy Econ 2012;15:25-32.
4. The Royal College of Psychiatrists of Thailand. Recommendations for the Pharmacotherapy of Mental Disorders. J Psychiatr Assoc Thailand 2013;58:221-32.
5. Lin L, Zhao YJ, Zhou HJ, Khoo AL, Teng M, Soh LB, *et al*. Comparative cost-effectiveness of 11 oral antipsychotics for relapse prevention in schizophrenia within Singapore using effectiveness estimates from a network meta-analysis. Int Clin Psychopharmacol 2016;31:84-92.
6. Gautam S, Meena PS. Drug-emergent metabolic syndrome in patients with schizophrenia receiving atypical (second-generation) antipsychotics. Indian J Psychiatr 2011;53:128-33.
7. World Health Organization. The Selection and Use of Essential Medicines: Report of the WHO Expert Committee, Italy; 2013.
8. Potkin SG, Saha AR, Kujawa MJ, Carson WH, Ali M, Stock E, *et al*. Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. Arch Gen Psychiatr 2003;60:681-90.
9. Farah A. Atypicality of atypical antipsychotics. Prim Care Companion J Clin Psychiatr 2005;7:268-74.
10. Kerwin R, Millet B, Herman E, Banki CM, Lublin H, Pans M, *et al*. A multicentre, randomized, naturalistic, open-label study between aripiprazole and standard of care in the management of community-treated schizophrenic patients schizophrenia trial of aripiprazole: (STAR) study. Eur Psychiatr 2007;22:433-43.
11. Drug and Medical Supply Information Center. In: Ministry of Public Health Thailand, editor. Reference of Drug Costs (Updated 24 May 2017); 2017.
12. Subcommittee of Development of National Drug List Thailand. Handbook of Health Technology Assessment for Thailand. 2nd ed. Nonthaburi: Watcharin P.P. Printing; 2013.
13. Robinson DG, Gallego JA, John M, Petrides G, Hassoun Y, Zhang JP, *et al*. A randomized comparison of aripiprazole and risperidone for the acute treatment of first-episode schizophrenia and related disorders: 3-Month outcomes. Schizophr Bull 2015;41:1227-36.
14. Truven Health Analytics Micromedex solutions. Risperidone; 2017. Available from: http://www.micromedexsolutions.com/

micromedex2/librarian/CS/46D719/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/62B8F8/ND_PG/evidencexpert/ ND_B/evidencexpert/ ND_AppProduct/evidencexpert/ND _T/evidencexpert/ PFActionId/evidencexpert.DoIntegratedSearch? SearchTerm=risperidone&UserSearchTerm=risperidone&SearchFilter= filterNone&navitem=searchALL#. [Last accessed on 2017, Mar 29]

15. Truven Health Analytics Micromedex solutions. Aripiprazole 2017 Available from: http://www.micromedexsolutions.com/micromedex2/librarian/CS/E3454C/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/C1E63C/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=aripiprazole&UserSearchTerm=aripiprazole&SearchFilter= filterNone&navitem= searchALL#. [Last accessed on 2017, Mar 29]
16. National Institute for Health and Care Excellence. Psychosis and Schizophrenia in Adults: Prevention and Management Clinical Guideline; 2014.
17. Columbia University Medical Center. Better options for people with treatment-resistant schizophrenia: Research on the comparative effectiveness of antipsychotic medications. Sci Daily 2015. Available from: https://www.sciencedaily.com/releases/2015/11/151106062315.htm. [Last accessed on 2016, Dec 24]
18. Davies A, Vardeva K, Loze JY, L'Italien GJ, Sennfalt K, Baardewijk MV. Cost-effectiveness of atypical antipsychotics for the management of schizophrenia in the UK. Curr Med Res Opin 2008;24:3275-85.
19. Sonnenberg FA, Beck JR. Markov models in medical decision making: A practical guide. Med Decis Making 1993;13:322-38.
20. National Statistical Office Ministry of Information and Communication Technology. Statistical Yearbook Thailand; 2016. p. 14-31.
21. Hatta K, Sato K, Hamakawa H, Takebayashi H, Kimura N, Ochi S, *et al*. Effectiveness of second-generation antipsychotics with acute-phase schizophrenia. Schizophr Res 2009;113:49-55.
22. World Health Organization. World Health Statistics 2016: Monitoring Health for the SDGs, Sustainable Development Goals. France: World Health Organization; 2016.
23. Srithanya Hospital Thailand. Report of the Reference Cost; 2017.
24. Standard Cost Lists for Health Technology Assessment; 2009. Available from: http://www.costingmenu.hitap.net. [Last cited on 2016 Dec 24].
25. Phanthunane P, Vos T, Whiteford H, Bertram M. Health outcomes of schizophrenia in Thailand: Health care provider and patient perspectives. Asian J Psychiatr 2010;3:200-5.
26. Sassi F. Calculating QALYs, comparing QALY and DALY calculations. Health Policy Plan 2006;21:402-8.
27. Williams L, Robinson S, Dickinson H. Rationing in Health Care: The Theory and Practice of Priority Setting. Bristol: The Policy Press; 2012.
28. Subcommittee of Development of National Drug List Thailand. Handbook of Health Technology Assessment for Thailand. Nonthaburi: The Graphico Systems Co., Ltd.; 2009.
29. Chan HY, Lin WW, Lin SK, Hwang TJ, Su TP, Chiang SC, *et al*. Efficacy and safety of aripiprazole in the acute treatment of schizophrenia in Chinese patients with risperidone as an active control: A randomized trial. J Clin Psychiatr 2007;68:29-36.
30. Park T, Kuntz KM. Cost-effectiveness of second-generation antipsychotics for the treatment of schizophrenia. Value Health 2014;17:310-9.
31. Komossa K, Rummel-Kluge C, Schwarz S, Schmid F, Hunger H, Kissling W, *et al.* Risperidone versus other atypical antipsychotics for schizophrenia. Cochrane Database Syst Rev 2011;1:CD006626.