

Cost Analysis of the Treatment of Schizophrenia in Thailand: A Simulation Model Comparing Olanzapine, Risperidone, Quetiapine, Ziprasidone and Haloperidol

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Objectives: To compare the annual costs of treating schizophrenia with four atypical antipsychotics-olanzapine, risperidone, quetiapine and ziprasidone and one typical antipsychotic: haloperidol in Thailand.

Material and Method: The present study used a cost analysis model. The model simulated treatment of schizophrenics for 12 months with the data from international literature review. A comprehensive search of pharmacoeconomic literature was carried out in order to identify studies to be included in the present review. Model parameter used data from the searches of 1175 publications but merely 31 of them were relevant to the objectives of the present study. Costs associated with olanzapine, risperidone, quetiapine, ziprasidone and haloperidol therapy were calculated over a period of 12-months. This analysis included health care costs and costs associated with productivity losses.

Results: The total cost from the cost analysis was as follows: Haloperidol gives the lowest annual cost of THB 86,004, within the atypical antipsychotics, Olanzapine produces an annual cost of THB 103,225 compared to THB 104,564 with risperidone, 118,314 with ziprasidone. The cost ranges up to THB 146,526 for quetiapine therapy.

Conclusion: Treatment with olanzapine appears to be more cost-effective than that with the other atypical antipsychotics in Thai schizophrenic patients.

Keywords: Cost analysis, Schizophrenia, Atypical antipsychotics, Olanzapine, Risperidone, Ziprasidone, Quetiapine, Haloperidol

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Schizophrenia is one of the most devastating of the psychiatric illnesses and it has significant economic and social effects⁽¹⁾. It affects approximately 1% of the population worldwide⁽²⁾. It causes lifelong suffering, prohibiting the patient from leading a normal and productive life, shortening life expectancy by ten years, and resulting in the suicide of one in every ten patients (World Health Report, 2001)⁽³⁾. Schizophrenia progressively impairs the personal, domestic, social and occupational ability of patients. This results in

poor self-care, rejection by the family and society, unemployment and dependence on others.

Atypical antipsychotic drugs alleviate the positive symptoms of schizophrenia as effectively as typical antipsychotics⁽⁴⁾. They also alleviate negative and depressive symptoms and cause fewer extrapyramidal side-effects than typical antipsychotics. Their cost is extremely high compared with conventional antipsychotics⁽⁵⁾, so its efficacy and low side effect has to be cost concerned for the 'care-providers' perspective and that of the patients who pay for it.

The authors therefore carried out this cost analysis study to compare atypical antipsychotics-

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olanzapine, risperidone, quetiapine, and ziprasidone - which have been marketed in Thailand with typical antipsychotic, haloperidol, in the treatment of schizophrenia.

Material and Method

This was an economic evaluation study using a cost analysis model. The model simulated treatment of schizophrenics for 12 months with the data from international literature review. Model parameter estimation was based on reviews of clinical trial data, other published medical literature and clinical judgment in the treatment of schizophrenia from the perspective of the healthcare. They can apply to Thai schizophrenic patients.

Search Strategy

Searches were performed by three electronic databases: Embase (1988 to 2003 Week 42), Medline (1966 to October Week 2, 2003), and the National Health Service Economic Evaluations Database (NHS EED). The following search string was applied to NHS EED: schizophrenia AND (economic or cost) AND (antipsychotic or atypical or typical or drug or medication or treatment). The result of the searches was 1175 publications (after excluding duplicates) but only 31⁽⁶⁻³⁶⁾ of them were relevant to the objectives of the present study. The results of this review was composed of a conclusion and synthesis of the findings in these studies.

Economic Model

Economic evaluations that focus on the short-term, either by design or because of lack of high-quality evidence, are likely to underestimate economic and clinically important outcomes, such as relapse rates and long-term compliance. Because of the long-term nature of schizophrenia, with its relapsing course and potential for long-term healthcare costs, short-term randomized controlled trials are unlikely to provide a fair and reasonable assessment of the full economic benefits of a new intervention. In each period the result of the efficacy - BPRS, PANSS, PANSS negative and PANSS positive - will be compared between olanzapine, risperidone, quetiapine, and ziprasidone.

Cost Analysis

Local unit costs associated with olanzapine, risperidone, quetiapine, and ziprasidone expressed in Thai baht were calculated over a period of 12-months. The analysis included all direct and indirect healthcare

costs including those associated with loss of productivity.

Medical Cost

Antipsychotics

The daily defined dose (DDD) of haloperidol is 8 mg, quetiapine 400 mg, ziprasidone 80 mg, risperidone 5 mg and olanzapine 10 mg. These doses have been used in the present analysis, except in the case of risperidone where a dose of 4 mg has been used to reflect local practice. In the analysis, the daily drug costs have been estimated using tablet strength, pack size, pack price and the DDD. The daily costs were then used to calculate the cost of medication for one year.

Anticholinergics

In Thailand, people requiring anticholinergic medication for drug-induced EPS are usually prescribed benzhexol tablets. The average cost was calculated in the same way as for antipsychotic medication.

Hospitalization Costs

Length of hospital stay of patients receiving different antipsychotics was reviewed by Foster and Goa (1999)⁽³⁷⁾. These antipsychotics included olanzapine, risperidone and haloperidol. No data on the cost of hospitalization for patients on quetiapine or ziprasidone are available. Hospitalization rate of risperidone had been used as an approximation for both quetiapine and ziprasidone.

Relapse Costs

Schizophrenia is a chronic psychiatric illness. Relapse is common even under optimum circumstances, with an average patient relapsing at least once every one to two years. Since data were not available on the number of relapses, it was therefore assumed that each patient would have one relapse. The data have been combined to estimate the cost of relapse.

Productivity Losses Due to Unemployment

Cost of unemployment calculated from the difference between the proportion of adults in the general population of Thailand who were in employment and the estimated employment rate for patients on each therapy reported by Foster and Goa (1999)⁽³⁷⁾.

Productivity Losses Due to Suicide Gestures or Attempts

The lost productivity resulting from suicide attempts was estimated by assuming that each patient

who attempts suicide would stop work, either due to success in suicide or due to hospitalization and rehabilitation. The average monthly earnings (THB 7,038) were used to estimate the loss of production. The figure was adjusted to take account of the fact that employment is very low among schizophrenic patients. Therefore, the chance of a patient being in employment has been used as the employment rate among schizophrenia patients.

Results

Efficacy and Tolerability of Antipsychotics

Olanzapine showed a better overall safety and efficacy status in longer-term trials, compared with both risperidone and haloperidol. None of the pooled outcomes measured, in both short-term and longer-term trials, were significantly in favor of the direct comparators (risperidone and haloperidol) or the indirect comparators (quetiapine or ziprasidone) compared to olanzapine. In both the short-term trials (< 12 weeks), anticholinergic use was significantly less in the olanzapine group than in the risperidone or haloperidol treatment groups. In addition, there was significantly less anticholinergic use in longer-term trials (> 12 weeks) within the olanzapine group compared with the risperidone, haloperidol, quetiapine or ziprasidone

treatment groups, indicating a better overall EPS profile for olanzapine (Table 1).

Medical Cost

Haloperidol had the lowest annual cost; THB 5,733, when compared with all the whole groups. Among the atypical antipsychotic group, risperidone had the lowest cost (THB 43,800) whereas quetiapine had the highest cost (THB 81,760). Annual cost of olanzapine and ziprasidone were THB 70,715 and THB 49,458, respectively. (Table 2) The rates of anticholinergic use in the controlled trials are shown in Table 3. Haloperidol had the highest cost of anticholinergic drug use and the lowest anticholinergic cost was the quetiapine group.

The rates of anticholinergic medication use for EPS in the randomised controlled trials. These rates were used for the economic evaluation. The costs resulting from the use of anticholinergic medication are shown in Table 3, for each medication.

Foster and Goa (1999)⁽⁴⁰⁾ examined the length of stay in hospital with different antipsychotics from a review of comparable randomized clinical trials. Patients treated with haloperidol spent an average of 67.4 days per year in hospital, compared with 53.7 days per year for those treated with olanzapine. Those receiving

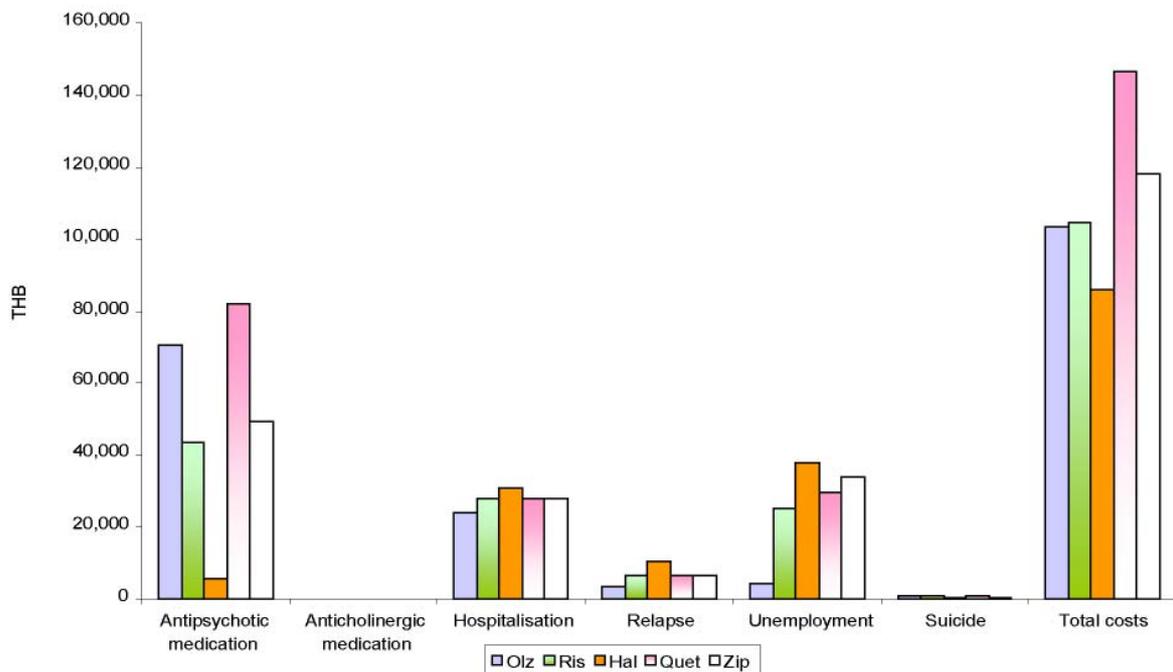


Fig. 1 These costs are presented graphically

Table 1. Efficacy and Tolerability of Antipsychotics

Outcome	OLZ vs RISP ¹		OLZ vs HAL		RISP vs HAL		OLZ vs QUET via HAL		OLZ vs ZIP via HAL	
	Risk Difference (95%CI)	p value	Risk Difference (95%CI)	p value	Risk Difference (95%CI)	p value	RDI-RD2 (95%CI)	p value	RDI-RD2 (95%CI)	p value
Short-term - dichotomous outcomes										
Anticholinergic use	-0.06 (-0.12, -0.01)	0.02*	-0.33 (-0.37, -0.30) ¹	<0.00001*	-0.21 (-0.31, -0.12) ^b	<0.001**	-0.10 (-0.39, 0.19)	0.503	0.06 (-0.19, 0.31)	0.642
Dropouts-any reason	-0.05 (-0.10, 0.01)	0.1	-0.14 (-0.22, -0.05) ²	0.002*	-0.06 (-0.10, -0.02) ^a	0.002**	-0.10 (-0.20, 0.00)	0.049*	-0.19 (-0.46, 0.08)	0.171
Dropouts-adverse events	-0.01 (-0.04, 0.03)	0.7	-0.03 (-0.05, -0.01) ¹	0.003*	-0.02 (-0.05, -0.01) ^a	0.11	0.02 (-0.05, 0.09)	0.590	0.00 (-0.12, 0.12)	1.000
Dropouts-lack of efficacy	0.00 (-0.03, 0.02)	0.8	-0.09 (-0.12, -0.06) ¹	<0.00001*	-0.03 (-0.07, 0.00) ^a	0.08	-0.13 (-0.18, -0.07)	0.0001*	-0.05 (-0.27, 0.17)	0.659
Long-term - dichotomous outcomes										
Anticholinergic use	-0.15 (-0.23, -0.07)	0.0003*	-0.51 (-0.83, -0.19) ²	0.002*	-	-	-0.50 (-0.93, -0.07)	0.023*	-0.41 (-0.75, -0.07)	0.019*
Dropouts-any reason	-0.12 (-0.22, -0.03)	0.008*	-0.20 (-0.34, -0.07) ¹	0.004*	-	-	0.17 (-0.22, 0.56)	0.388	-0.17 (-0.35, 0.01)	0.061
Dropouts-adverse events	-0.01 (-0.07, 0.05)	0.8	-0.07 (-0.15, 0.02) ¹	0.12	-	-	-0.06 (-0.36, 0.24)	0.696	0.01 (-0.10, 0.12)	0.854
Dropouts-lack of efficacy	-0.06 (-0.12, 0.01)	0.11	-0.10 (-0.19, -0.01) ¹	0.03*	-	-	0.15 (-0.14, 0.44)	0.317	-0.12 (-0.26, 0.02)	0.098

Table 1. Efficacy and Tolerability of Antipsychotics (continued)

Short-term - continuous outcomes										
	WMD (95%CI)	p value	WMD (95%CI)	p value	WMD (95%CI)	p value	WMD1- WMD2	p value	WMD1- WMD2	p value
PANSS total change	-0.86 (-3.82, 2.11)	0.6	-4.39 (-6.20, -2.57)	<0.00001*	-3.00 (-5.37, -0.64)	0.01**	-7.79 (-12.66, -2.92)	0.002*	-	-
PANSS positive change	0.39 (-0.60, 1.37)	0.4	-0.82 (-1.37, -0.26)	<0.00001*	-0.23 (-0.97, 0.51)	0.54	-	-	-	-
PANSS negative change	-0.31 (-1.23, 0.61)	0.5	-1.29 (-1.82, -0.75)	<0.00001*	-0.79 (-1.56, 0.01)	0.051	-	-	-	-
BPRS total change	-0.97 (-3.86, 1.92)	0.5	-2.59 (-3.67, -1.50)	<0.00001*	-1.63 (-3.06, -0.20)	0.03**	-3.50 (-8.11, 1.11)	0.137	-	-
Long-term - continuous outcomes										
PANSS total change	-5.35 (-10.15, -0.55)	0.03*	-9.96 (-17.99, -1.92)	0.02*	-	-	-2.26 (-24.18, 19.66)	0.840	-	-
PANSS positive change	0.81 (-2.01, 0.39)	0.19	-3.14 (-5.11, -1.18)	0.002*	-	-	-3.34 (-10.84, 4.16)	0.383	-	-
PANSS negative change	-1.39 (-2.66, -0.13)	0.03*	-1.21 (-3.26, 0.83)	0.25	-	-	1.89 (-3.24, 7.02)	0.470	-	-
BPRS total change	-3.23 (-6.00, -0.46)	0.02*	-7.08 (-11.61, -2.56)	0.002*	-	-	-	-	-	-

Abbreviations: CI, confidence interval; OLZ, olanzapine; PANSS, Positive and Negative Syndrome Scale; BPRS, Brief Psychiatric Rating Scale; RIS, risperidone
WMD, Weighted mean difference

¹Fixed effects model. ²Random effects model

*Significantly in favour of olanzapine, **significantly in favour of risperidone

Table 2. Medical Cost

	Olan		Risp		Hal		Quet		Zip		Benz		
Strength (mg)	5	10	1	2	0.2	2	5	100	200	20	40	2	5
Number (per pack)	28	28	60	60	250	100	100	30	30	20	20	500	500
Strength per pack (mg)	140	280	60	120	125	200	500	3000	6000	400	800	1000	2500
Daily defined dose (mg)	10	10	4	4	8	8	8	400	400	80	80	6	6
Price per pack (THB)	2,782	5,286	2,040	3,120	370	328	645	1,935	2,850	1,740	1,940	100	160
Daily cost (THB)	198.7	188.8	136.0	104.0	23.7	13.1	10.3	258.0	190.0	174.0	97.0	0.6	0.4
Average daily cost (THB)	193.7		120.0		15.7		224.0		135.5		0.5		
Annual cost (THB)	70,715		43,800		5,733		81,760		49,458		179.6		

Table 3. Total costs of anticholinergic medication use

Therapy	Incidence of anticholinergic use	Total anticholinergic drug cost ^a (THB)
Olanzapine	18.5%	33.22
Risperidone	39.0%	70.04
Haloperidol	64.3%	115.53
Quetiapine	15.0%	26.94
Ziprasidone	40.0%	71.83

^aTotal cost = rate of anticholinergic use x twelve-monthly drug cost. Assuming 100% compliance one year cost is THB 180

risperidone were hospitalised for an average of 4.5 days per month (54.0 days per year), compared with 3.9 days per month (46.8 days per year) for olanzapine patients. No data are available regarding hospitalisations for quetiapine or ziprasidone. Although risperidone is likely to have greater efficacy than quetiapine and ziprasidone, the risperidone hospitalisation rate has been used as an approximation for both.

The full cost of one day in hospital in Thailand is THB 513, according to the Ministry of Public Health. Using this rate, the costs of hospitalisation have been calculated and are shown in Table 4.

With the total costs for each of the drugs that was presented in Table 5, haloperidol gave the lowest annual cost of THB 86,004, within the atypical antipsychotics, Olanzapine produces an annual cost of THB 103,225 compared to THB 104,564 with risperidone, 118,314 with ziprasidone. The cost ranges up to THB 146,526 for quetiapine therapy.

Discussion

Many costs are associated with the treatment for schizophrenia. These can be separated into direct and indirect costs. Direct costs are the value of health care resources used to treat schizophrenia, including cost of antipsychotic drugs, cost of anticholinergic use, hospital admissions and relapse cost.

Indirect costs comprise lost productivity by means of patients who are unemployed as a result of schizophrenia. Schizophrenia also places an additional burden on the family and on society in terms of the time taken in caring for the patient. Placing a value on this care is difficult and is, therefore not included. Additional productivity losses occur through suicide, which is a devastating event for society and especially for the family of the patient.

According to the World Health Organization (WHO), the daily defined dose (DDD) is 8 mg for haloperidol, 400 mg for quetiapine, 80 mg for ziprasidone,

Table 4. Non-medical cost

	Olan	Risp	Hal	Quet	Zip
Cost of hospital stay					
Annual length of stay (days) ^a	46.8	54.0	60.5 ^c	54.0	54.0
Total hospitalization cost (THB) ^b	24,008	27,702	31,037	27,702	27,702
Cost of relapse per year					
Relapse risk (%) ^d	14.4	24.1	33.8	24.1	24.1
Annual length of stay (days) ^a	46.8	54.0	60.5	54.0	54.0
Total hospitalization cost (THB) ^c	3,457	6,676	10,490	6,676	6,676
Unemployment cost					
Employment rate (%) ^a	19.0	13.5	8.0	13.5	13.5
Chance of returning to employment (%) ^f	50	25	10	20	15
Rate of employment loss (%) ^g	5.1	30.1	45.1	35.1	40.1
Productivity loss (THB) ^h	4,315	25,429	38,097	29,651	33,874
Cost due to suicide					
Rate of suicidal attempt (%) ^a	1.7	4.2	6.3	4.2	4.2
Productivity loss (THB) ⁱ	696.8	886.8	532.1	709.4	532.1
Total annual cost	32,477	60,694	80,156	64,738	68,784

^aSource: Foster and Goa (1999)⁽³⁷⁾

^bThe cost of a hospital stay is THB 513 per day. Total hospital cost = length of stay x THB 513

^cThe length of stay for patients on haloperidol was imputed from the extra advantage olanzapine offered over haloperidol (ie, 13.7 days)

^dSource: Ascher-Svanum et al (2004)⁽³⁸⁾

^eCost of hospital stay is THB 513 per day. Total hospital cost = relapse risk x length of stay x relapses per year x THB 513

^fEstimate
^gEmployment rate is 55.1% in Quarter 2, 2004 (National Statistical Office Thailand website http://www.nso.go.th/eng/stat/lfs_e/lfs_e-tab7.xls). The employment rate loss due to schizophrenia = the employment rate – chance of returning to employment for each antipsychotic therapy

^hAverage monthly earnings of THB 7038 (Quarter 2, 2004) sourced from National Statistical Office

ⁱLost productivity = attempt rate x chance of returning to employment x annual earnings. Average monthly wage is THB 7038, (annual earnings THB 84,456)

Note: Unemployment in Thailand is currently 2.3% (from National Statistical Office), which is probably lower than in the countries used in Foster and Goa (1999)⁽³⁷⁾, however the differences should remain valid

Table 5. Comparison of annual total costs

Cost item	Olan	Risp	Hal	Quet	Zip
Antipsychotic medication (THB)	70,715	43,800	5,733	81,760	49,458
Anticholinergic medication (THB)	33	70	116	27	72
Hospitalisation (THB)	24,008	27,702	31,037	27,702	27,702
Relapse (THB)	3,457	6,676	10,490	6,676	6,676
Unemployment (THB)	4,315	25,429	38,097	29,651	33,874
Suicide (THB)	697	887	532	709	532
Total costs	103,225	104,564	86,004	146,526	118,314

5 mg for risperidone and 10 mg for olanzapine. These doses have been used for this analysis, except for risperidone where a dose of 4 mg has been used, reflecting local practice. In the analysis, the daily drug costs have been estimated using tablet strength, pack size, pack price and the DDD. The daily costs have then been used to calculate the cost for one year (by multiplying the daily cost by 365).

For the cost of non medical cost as shown in Table 4, haloperidol had the highest cost (THB 80, 156). Ziprasidone, quetiapine, risperidone were lower respectively whereas olanzapine had the lowest non medical cost. That is because olanzapine has a shorter length of stay, lower relapse risk, lower suicidal rate and higher employment rate from the outcome of the clinical trial. The lowest non medical cost of olanzapine led to the lowest annual total cost of olanzapine among the atypical antipsychotics in the treatment of schizophrenia.

Patients with schizophrenia frequently relapse, particularly if their illness is not well controlled or they do not comply properly with treatment. Relapse is a considerable cost factor. Data obtained from Ascher-Svanum et al (2004)⁽³⁸⁾ indicate the relapse rate of patients on olanzapine and risperidone. Since haloperidol data were not collected by these authors, it has been assumed that risperidone represents a mid-point in the olanzapine: haloperidol range for patients on conventional antipsychotics. Data from Csernansky et al (2002)⁽³⁹⁾ suggest that such a method is conservative. Data are not available regarding the length of inpatient stay if patients relapse, so it has been assumed for the purpose of the present study that the hospital stay reported by Foster and Goa (1999)⁽³⁷⁾ is maintained.

The results of the economic analyses support the clinical analyses presented in Table 1. The clinical analyses suggest that olanzapine is superior to risperidone, quetiapine, ziprasidone and haloperidol, particularly in the medium- to long-term, with regard to treatment (both positive and negative symptoms), incidence of EPS and drop-out rate.

Conclusion

With the model simulated treatment of schizophrenics for 12 months used the data from the international literature review. The authors' analyses show that, in Thailand, olanzapine is a cost-effective alternative to risperidone, quetiapine, and ziprasidone for the treatment of schizophrenia within atypical antipsychotics. They demonstrate that the savings of

other resources used to manage schizophrenia outweigh the additional acquisition cost of olanzapine. The benefits to society of using olanzapine in Thai schizophrenic patients was suggested by this the present study so it can give efficient use of the resources.

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การวิเคราะห์ต้นทุน การรักษาโรคจิตเภทในคนไทย: เปรียบเทียบระหว่างยา โอลานซาปิน ริสเพอริดอล คิวไทอาปิน ซิปราซิโดน และ ฮาโรเพอริดอล

รณชัย คงสกนธ์, ธวัชชัย ลิพินาจ

วัตถุประสงค์: เพื่อเปรียบเทียบ ค่ารักษาผู้ป่วยจิตเภทในระยะเวลา 1 ปี ระหว่างการ รักษาด้วยยาต้านโรคจิต atypical 4 ชนิดโอลานซาปิน ริสเพอริดอล คิวไทอาปิน ซิปราซิโดน และ ยาต้านโรคจิต typicalฮาโรเพอริดอล

วัสดุและวิธีการ: การศึกษานี้ใช้ แบบแผน วิเคราะห์ ต้นทุนการรักษาระยะเวลา 1 ปี โดยการสืบค้นวรรณกรรมวิจัยทางเศรษฐศาสตร์ที่เกี่ยวข้อง 1175 การวิจัย โดยมี 31 งานวิจัยที่เกี่ยวข้อง นำผล มาวิเคราะห์เชิงเศรษฐศาสตร์ โดย ศึกษามูลค่าการรักษาและ มูลค่าที่เกี่ยวกับการสูญเสียรายได้จากการเจ็บป่วยซึ่งเป็นข้อมูลศึกษาจากต่างประเทศ โดยเป็นข้อมูลที่มีหลักฐานทางวิชาการ สามารถนำมาใช้เปรียบเทียบในผู้ป่วยจิตเภทคนไทย

ผลการศึกษา: จากการวิเคราะห์ต้นทุนทั้งหมด ฮาโรเพอริดอลมีต้นทุนต่ำสุดที่ 86,004 บาท ต่อปี ในกลุ่มยา ต้านโรคจิต atypical โอลานซาปิน มีต้นทุนต่ำสุดที่ 103,225 บาท ต่อปี ตามด้วย ริสเพอริดอลที่ 104,564บาท ต่อปี ซิปราซิโดน 118,314 บาท ต่อปี คิวไทอาปิน146,526 บาท ต่อปี ตามลำดับ

สรุป: การรักษาโรคจิตเภทในคนไทยด้วยกลุ่มยาต้านโรคจิต atypical ยาโอลานซาปิน เป็นกลุ่มยาที่มีความคุ้มทุนในเชิงเศรษฐศาสตร์มากกว่า เมื่อเปรียบเทียบกับตัวอื่นในกลุ่มเดียวกัน
