

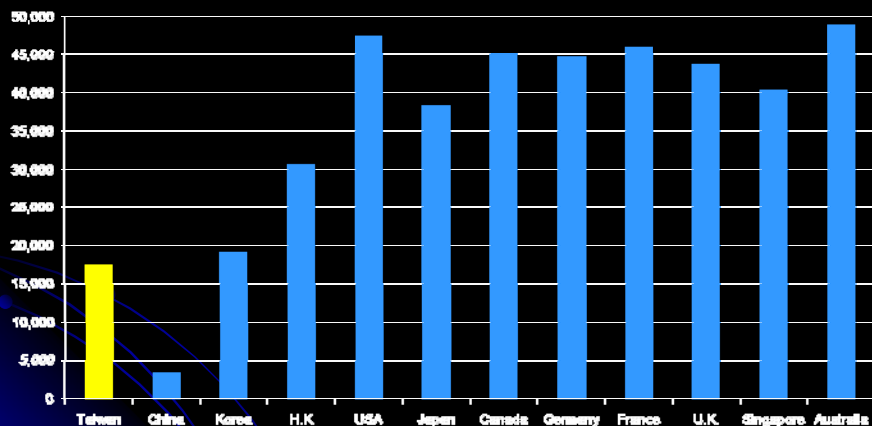
Pharmacoeconomic evaluation of newer atypical antipsychotics and bipolar disorder

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2008 Gross Domestic Product Per Capita

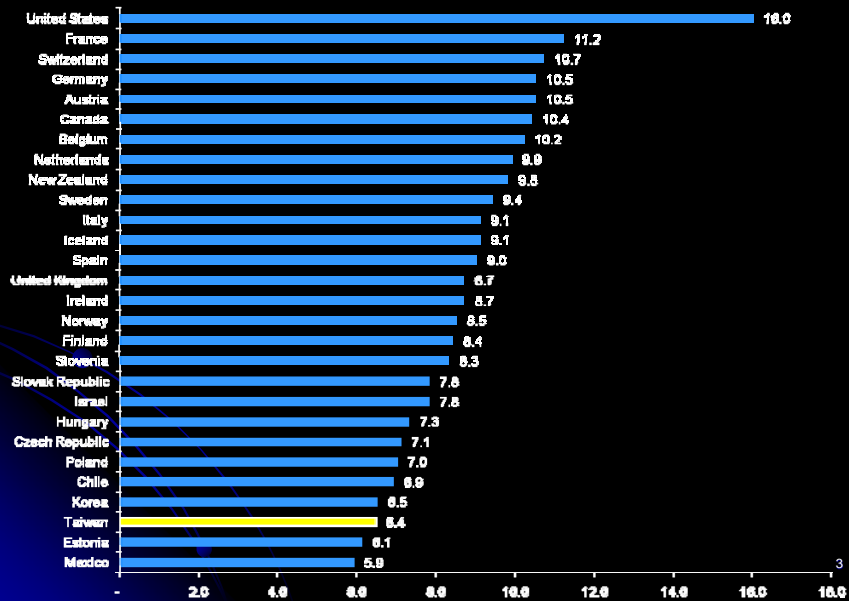


Unit: USD

國際貨幣基金會(IMF) 國際金融統計(IFS) ; June 2008

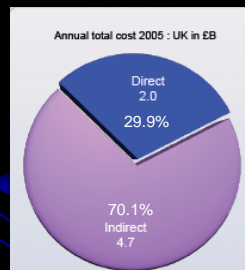
Percentage of Medical Demand in GDP

GDP as % of NHE (2008)

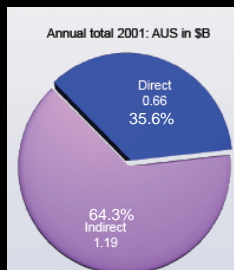


Direct and Indirect Costs

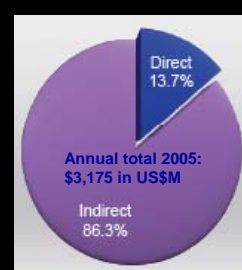
UK



Australia



Korea



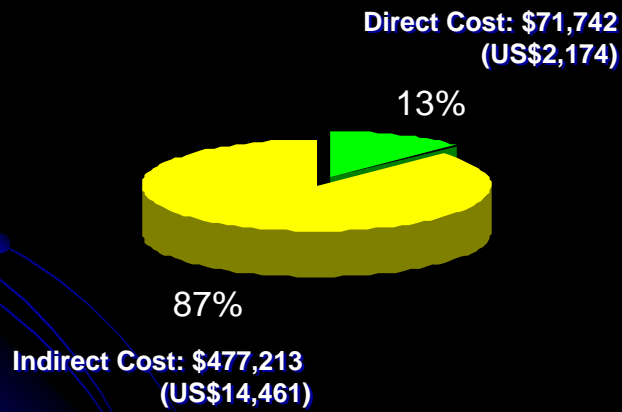
- Unemployment was identified as the largest component of overall cost ⁴

¹ Mangalore, R. et al. (2007). J Ment Health Policy Econ, 10(1), 23-41.

² Access Economics: SANE Australia 2002

³ Chang, S. M. et al. (2008). J Korean Med Sci, 23(2), 167-175.

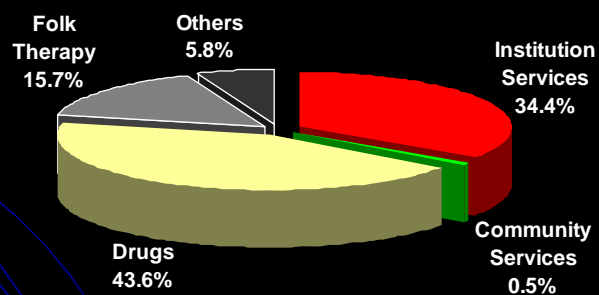
The average cost for each patients with schizophrenia in Taiwan



(Lee et al Psychiatr Res 2008)

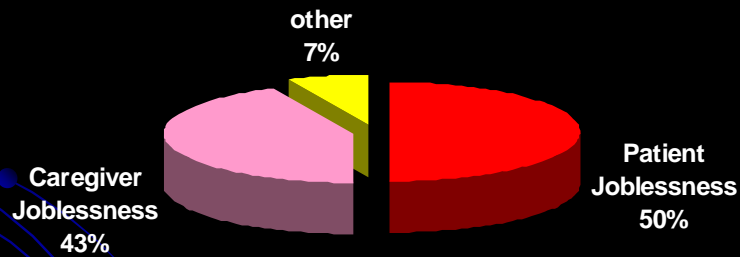
Direct costs

Non-psychiatric medical services



(Lee et al Psychiatr Res 2008)

Indirect cost



(Lee et al Psychiatr Res 2008)

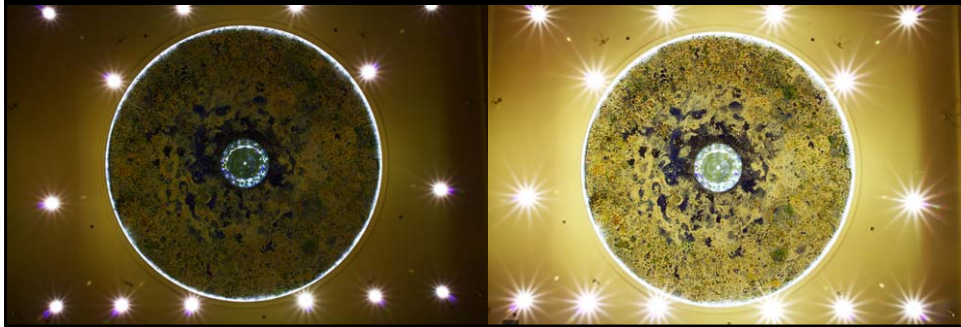
Three tasks for pharmacoeconomic evaluation

- 1. Long acting risperidone (**Consta**)
 - Yang YK et al Psychiatry and Clinical Neuroscience 2005; 138:385-94
- 2. Paliperidone oral tablet (**Invega**)
 - Puw RF et al Taiwanese J of Psychiatry 2010;24:280-90
- 3. Medical cost of bipolar disorder (**New indication**)
 - Tang et al Bipolar disorders 2010;35:107-10

Long acting risperidone (Consta)

Yang YK et al Psychiatry and Clinical Neuroscience 2005; 138:385-94

(成大醫院/蒼穹之窗)



Original Design

Flow chart (June 2003)

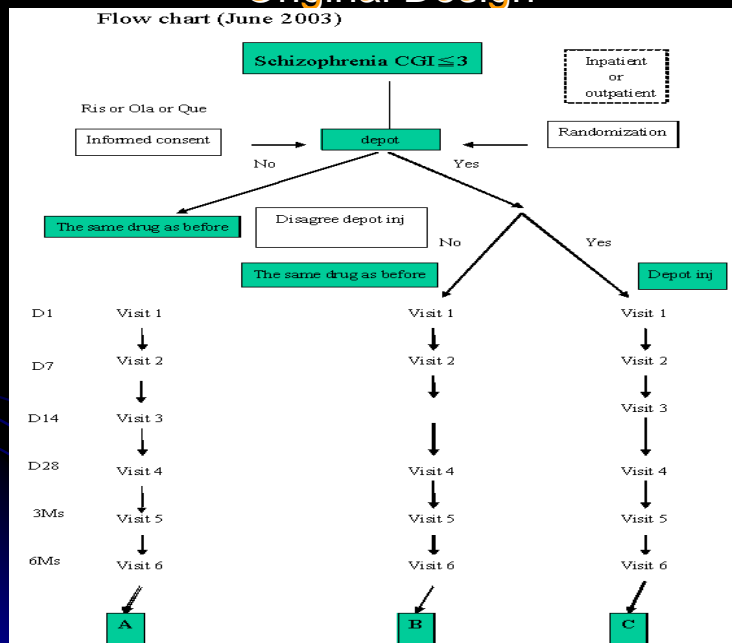
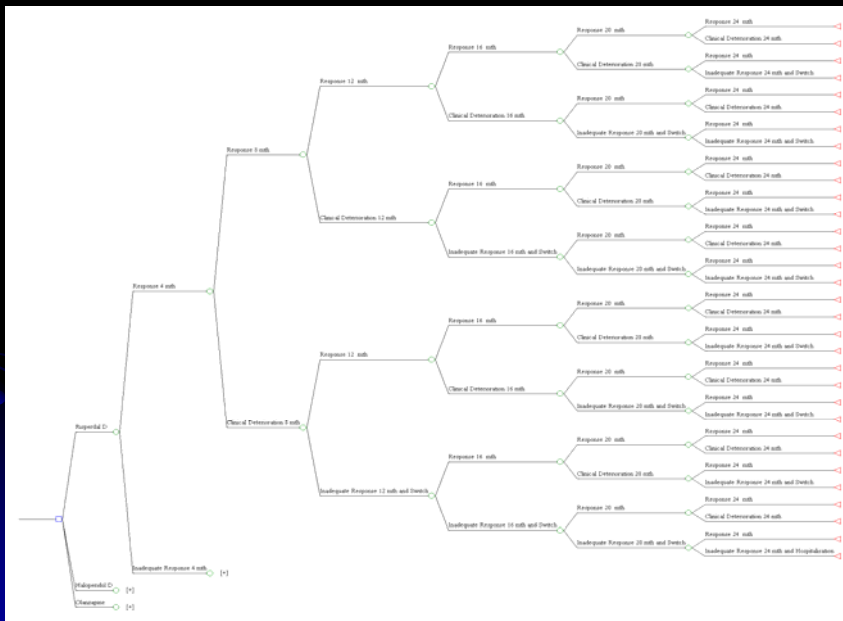


Diagram 1: Decision Tree –Depot Risperidone-”Response” Branch



Executive committee (expert opinion)

- 6 senior psychiatrists
- 2 **pharmacoeconomists** / statistic specialists
- 1 representative of pharmaceutical company

Probability of efficacy: by anonymous experts

- Clinical research agent (CRO)
- Their clinical experience in psychiatry is more than 15 years.
- Currently, they actively provide clinical services for schizophrenic patients, particularly inpatient service .
- Their administration load is minimal.
- They are not full-time child psychiatrists.
- They are not full time psychotherapists.
- The risperidone, depot haloperidol and olanzapine are available for more than 2 years in their hospital or institution.
- They are not members of the executive committee in this study.

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The therapeutic options in the model

Initial agents	Long-acting risperidone	Depot haloperidol	Olanzapine
1 st option	Olanzapine	Long-acting risperidone	Long-acting risperidone
2 nd option	Clozapine	Olanzapine	Clozapine
3 rd option	Depot haloperidol	Clozapine	Depot haloperidol

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Patient population

- BPRS<40
- Stable schizophrenics
- Duration of illness less than 5 years
- Age<35 yo

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The incidences of EPS and average dosage among different agents for different medical states

	EPS incidence	Dosage		
		R	CD	IR
Long acting risperidone	6%	25mg/14day	25mg/14day	37.5mg/14day
Oral risperidone	30%	3mg/day	4mg/day	6mg/day
Olanzapine	18%	15mg/day	17.5mg/day	20mg/day
Depot haloperidol	55%	100mg/28day	150mg/28day	200mg/28day
Clozapine	5%	35mg/day	425mg/day	450mg/day

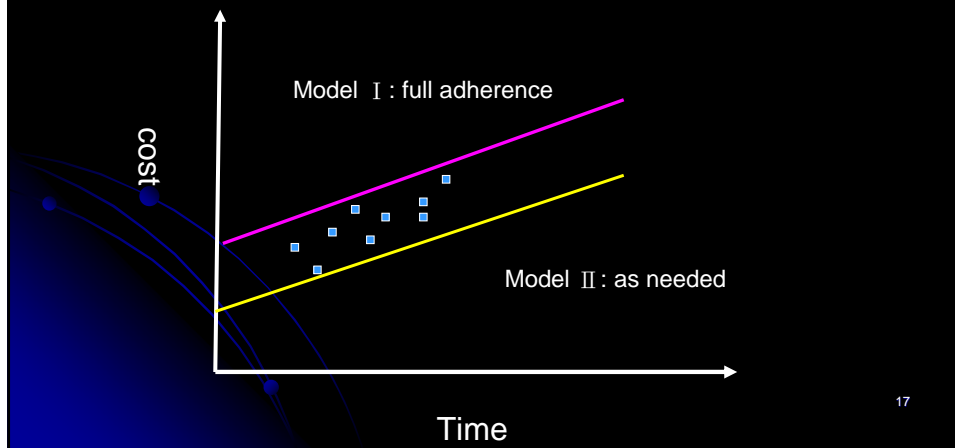
EPS: extrapyramidal side effect; CD: Clinical deterioration

R: Response ; IR: Inadequate response

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Estimated Cost

- Unit cost: 0.9% population of Taiwanese
- Four-month cost (treatment package)



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Table 3. The average four-month costs for different medical states in Models I and II

Cost items/medical status	Response		CD		IR	
	Model I	Model II	Model I	Model II	Model I	Model II
Outpatient clinic	1,898	1,447	1,239	839	1,119	757
Intensive care	8,578	—	84,637	23,901	101,993	37,939
Home care	412	38	412	77	348	1,021
Emergency service	165	—	768	1,471	906	1,120
Total costs	11,052	1,485	87,056	26,603	104,365	41,287

Unit: New Taiwan dollar (NT\$)

CD: Clinical deterioration

IR: Inadequate response

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Table 4. Models I and II: two-year cost-effectiveness analysis among three strategies

Strategies	Effectiveness	Costs(NT\$)		C/E ratio (NT\$)	
		Model I	Model II	Model I	Model II
Long-acting risperidone	0.55	374,187	252,885	678,367	458,457
Depot haloperidol	0.32	315,834	167,036	1,000,741	529,265
Olanzapine	0.45	381,285	244,055	841,875	538,872

NT\$: New Taiwan dollar

C/E: Cost-effectiveness

Table 5. Sensitivity analysis (Model I) of the impact of increasing the response rate of long-acting risperidone by 0%~15%

Probability	Cost (NT\$)			Effectiveness			Cost/Effectiveness (NT\$)		
	Risperidone long-acting	Haloperidol depot	Olanzapine	Risperidone long-acting	Haloperidol depot	Olanzapine	Risperidone long-acting	Haloperidol depot	Olanzapine
0.75 (-0%)	383,866	315,834	381,285	0.50	0.32	0.45	765,436	1,000,741	841,875
0.79 (-5%)	379,027	315,834	381,285	0.53	0.32	0.45	719,763	1,000,741	841,875
0.83 (-10%)	347,187	315,834	381,285	0.55	0.32	0.45	678,367	1,000,741	841,875
0.87 (-15%)	369,348	315,834	381,285	0.58	0.32	0.45	640,451	1,000,741	841,875

NT\$ New Taiwan Dollar

*The incremental response rate was added only at the first episode (the first 4 month of this trial).

Table 6. Sensitivity analysis (model I) of the impact of long-acting risperidone price variation by 0%~15%

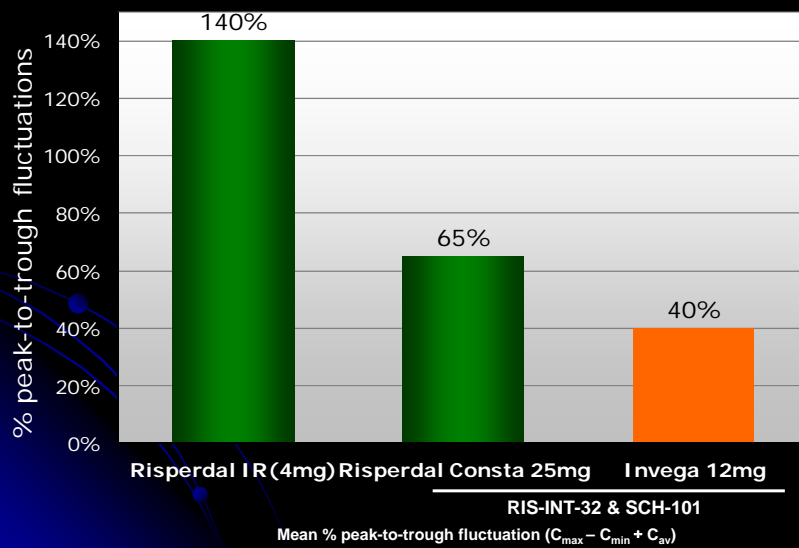
Constant Price (25mg; 37.5mg)	Cost (NTS)			Effectiveness			Cost/Effectiveness (NTS)		
	Risperidone long -acting	Haloperidol depot	Olanzapine	Risperidone long -acting	Haloperidol depot	Olanzapine	Risperidone long -acting	Haloperidol depot	Olanzapine
4,367; 5,895 (0%)	374,187	315,834	381,285	0.55	0.32	0.45	678,367	1,000,741	841,875
4,585; 6,190 (+5%)	382,357	318,964	383,449	0.55	0.32	0.45	693,178	1,010,659	846,653
4,804; 6,485 (+10%)	390,527	322,095	385,613	0.55	0.32	0.45	707,989	1,020,580	851,431
5,022; 6,779 (+15%)	398,697	325,226	387,777	0.55	0.32	0.45	722,801	1,030,501	856,209

NTS: New Taiwan dollar

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(Yang YK et al 2005)

INVEGA: Min. Peak-to-trough Fluctuation

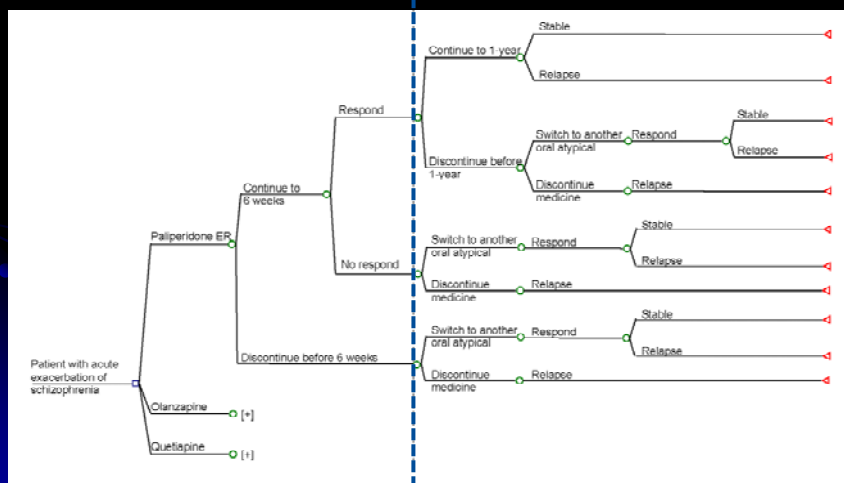


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Invega Cost-Effectiveness model

Acute model

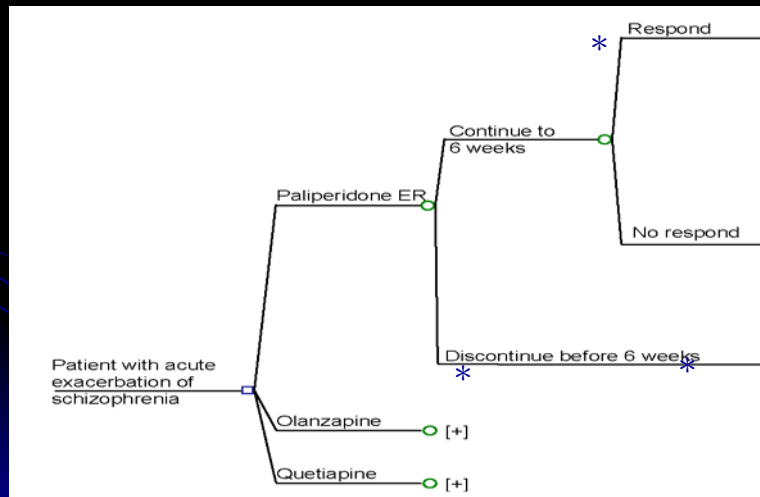
Long-term model



Study tasks

- Literature review
- To apply **National Health Insurance (NHI)** data of schizophrenia in 2005 from National Health Research Institute (unit cost of medical resource utilization)
- To conduct expert interview via structured questionnaire (N=10) : conducted by **CRO (日祥醫事管理公司)**
- To conduct **expert meeting** (N=4+2)

Acute model



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Acute model - 1

Table 1. Response rate in acute model

Comparator	Study Design	Dose	Definition of Response	Atypical Response Rate	Placebo Response Rate	Reference
Paliperidone ER	6-week, pts w/ sz & acute exacerb'n, olanzapine comparator	6mg/d	≥30% decrease in PANSS from bsln to study endpt	53.2%	27.4%	Marder (2007), Davidson (2007), Kane (2007)
Olanzapine	6-week, pts w/ sz & acute exacerb'n, paliperidone ER comparator	10mg/d	≥30% decrease in PANSS from bsln to study endpt	50.1%	27.4%	Marder (2007), Davidson (2007), Kane (2007)
Quetiapine	6-week, inpts w/ chronic or subchronic sz & acute exacerb'n	750mg/d	≥30% decrease in BPRS at any time during tmt	49.0%	35.0%	Arvanitis & Miller (1997)

Table 2. Normalized response rate in acute model

	Response rate (a)	Placebo response rate (b)	Absolute response rate (a-b)	Normalized response rate (A)	Normalized response rate - placebo (B)
Paliperidone ER	53.2%	27.4%	25.8%	55.8%	29.9%
Olanzapine	50.1%	27.4%	22.8%	52.7%	29.9%
Quetiapine	49.0%	35.0%	14.0%	43.9%	29.9%

Acute model - 2

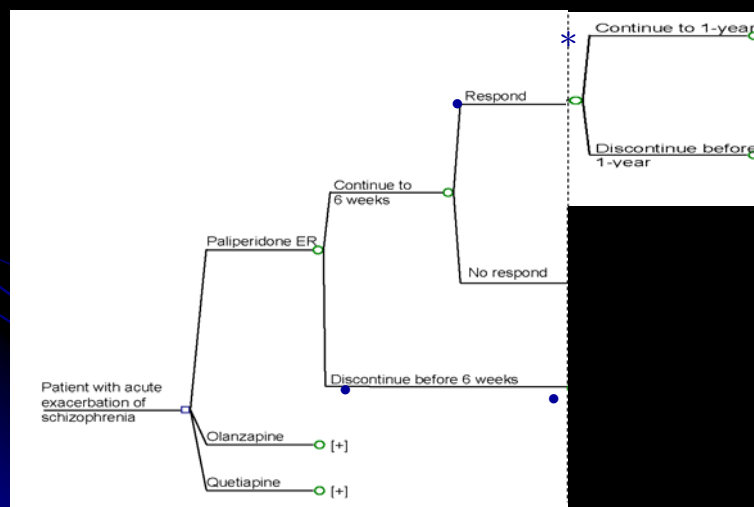
Table 3. Discontinuation rate within 6 weeks prior to receiving medication

	Discontinuation Rate	Source
Paliperidone ER	15%	Assumed equal to olanzapine and risperidone
Olanzapine	15%	CATIE study ²⁷
Quetiapine	18%	CATIE study ²⁷

- **30%** p't with discontinuation will seek medical help.

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Acute model + Long-term model (→)



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One-year treatment compliance

Risperidone : 68.3%

Olanzapine : 74.6%

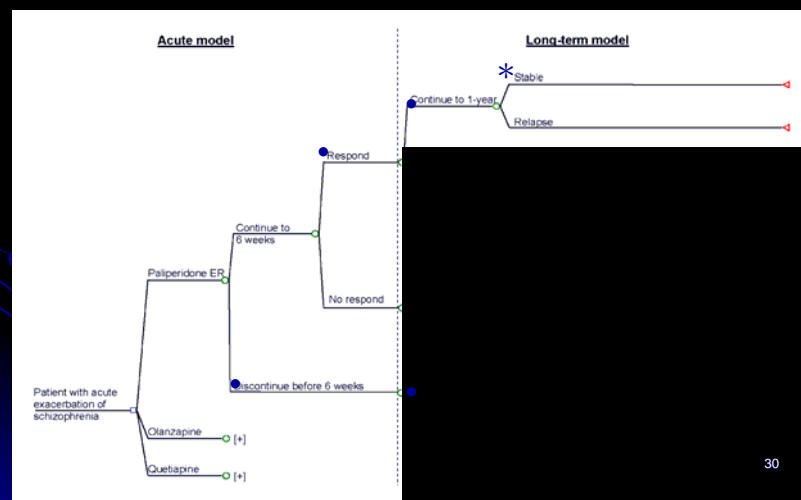
Quetiapine : 60.0%

Paliperidone : **73.3 %**

IC-SOHO

(Dossenbach et al J Clin Psychiatry 2005)²⁹

Acute model + Long-term model (\rightleftharpoons)

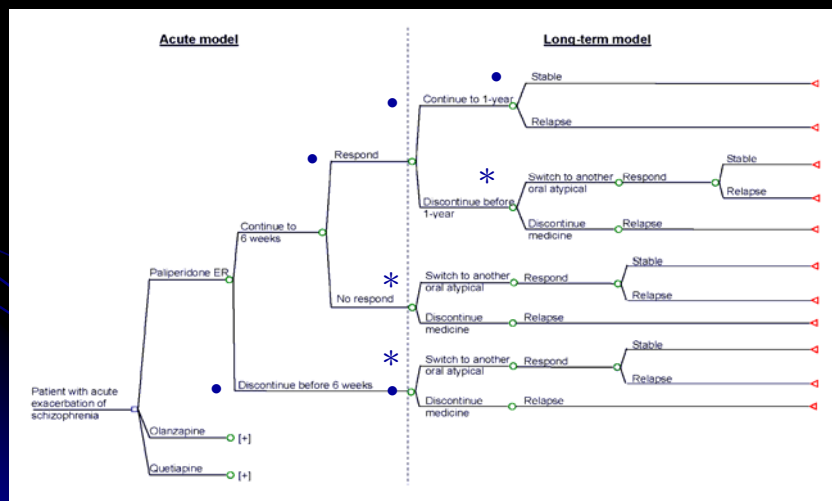


Long Term model (one year)

- Relapse/ worsen rate 20.2%~37.0% (N.S. 21.8%).
- Hospitalization rate 9.2% (NS)
- $21.8\% + 9.2\% = 31.0\%$ (Dossenbach etal 2005)
- The mean of hospitalization was 1.7 times per year (2005 NHRID)

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Acute model + Long-term model (三)

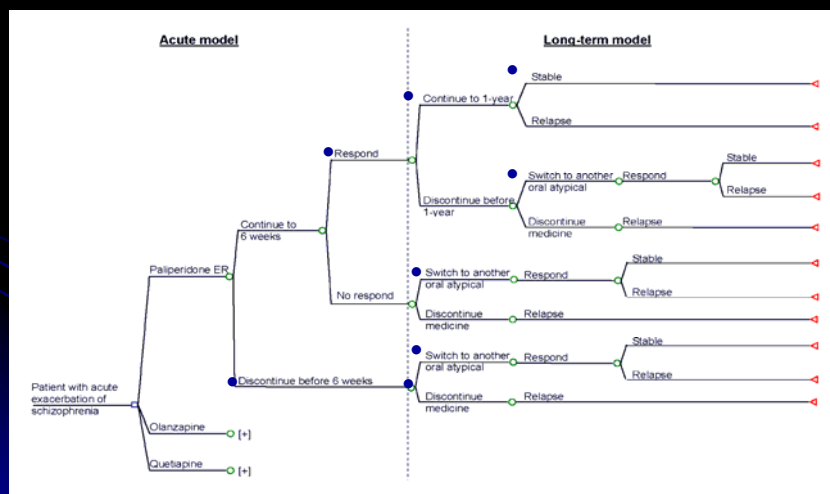


One-year model (三) — no response & switch

- Switch rate : **54.4%**
(California Medicaid data ; Menzin et al Psychiatry Service 2003, CATIE)

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Acute model + Long-term model (四)



Duration of switch

Table 4. Treatment duration under different condition

	First Medication (Months)	Switched Medication (Months)
Patients who respond & switch	6.0	6.0
Patients who don't respond & switch	2.0	6.0
Patients who discontinue by 6 weeks & switch	1.0	6.0

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Daily cost for drugs

Table 5. Daily cost for drugs

	Avg. daily dose	Avg. daily medication cost (NTD)
Paliperidone ER	6mg	166
Olanzapine	10mg	158
Quetiapine	750mg	259.8*

*Assumption: calculated from 300mg*1+200mg*2+25mg*2, 89NTD for 300mg, 65NTD for 200mg and 20.4NTD for 25mg (NHI price on Sep 1, 2007)

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EPS

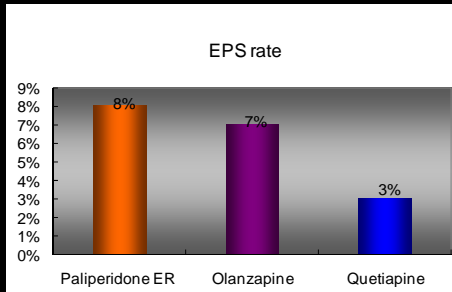


Table 6: Paliperidone 6 weeks trial-EPS related adverse event rate

Body system or organ class MedDRA preferred term	Placebo n=355	PALI ER 6mg n=235	Olanzapine 10 mg n=364
Total % of subjects with EPS-related AE	11%	10%	9%
Akathisia	4%	3%	2%
Extrapyramidal disorder*	2%	2%	2%
Tremor	3%	3%	2%
Hypertonia	1%	1%	1%
Dystonia	1%	1%	<1%
Dyskinesia	1%	<1%	<1%
Parkinsonism	0	<1%	1%
Muscle spasms	<1%	0	<1%
Oculogyration	0	0	0
Hyperkinesia	0	0	0
Drooling	<1%	1%	<1%
Muscle rigidity	0	0	0
Musculoskeletal stiffness	1%	0	0

Table 7: EPS rate in each group

	% Patients	Source	
Paliperidone ER	8.0%	Avg. EPS rate of olanzapine and risperidone in CATIE study	
Olanzapine	7.0%		CATIE study ²⁷
Quetiapine	3.0%		CATIE study ²⁷

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Average cost-effectiveness in acute phase

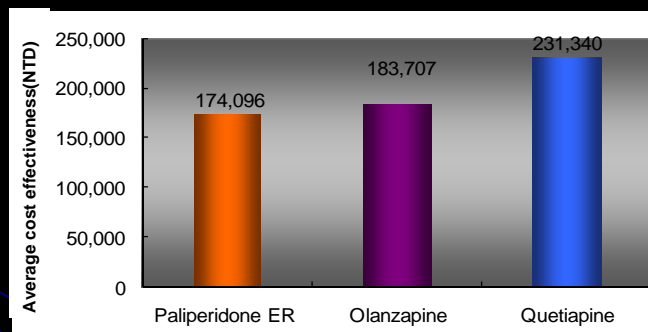


Table 8: Average cost effectiveness in acute model

	Effect: # of patients responding (per 100 patients)	Cost (per 100 patients)	Average C/E
Paliperidone ER	55.8	9,714,530	174,096
Olanzapine	52.7	9,681,361	183,707
Quetiapine	43.9	10,155,830	231,340

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Average cost-effectiveness in long-term phase

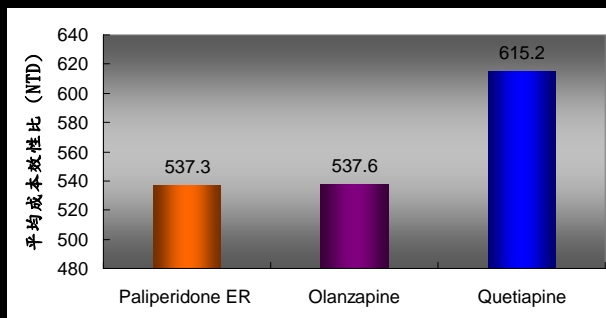
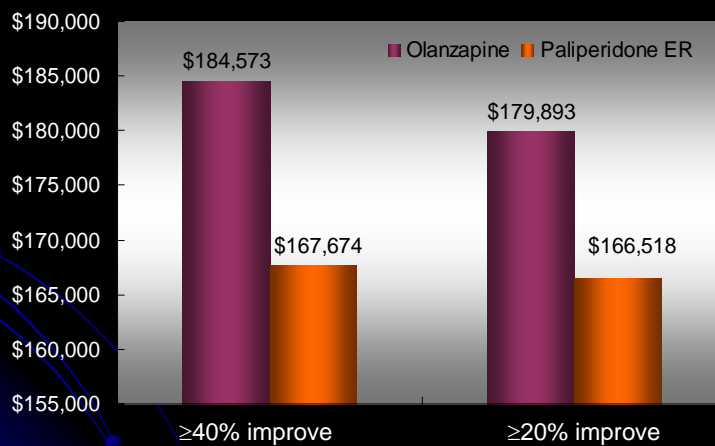


Table 10. Average cost effectiveness in long-term model

	Effect per 100 patients (stable days)	Cost (per 100 patients)	Average C/E
Paliperidone ER	31,459	16,903,121	537.3
Olanzapine	31,395	16,877,371	537.6
Quetiapine	30,830	18,965,543	615.2

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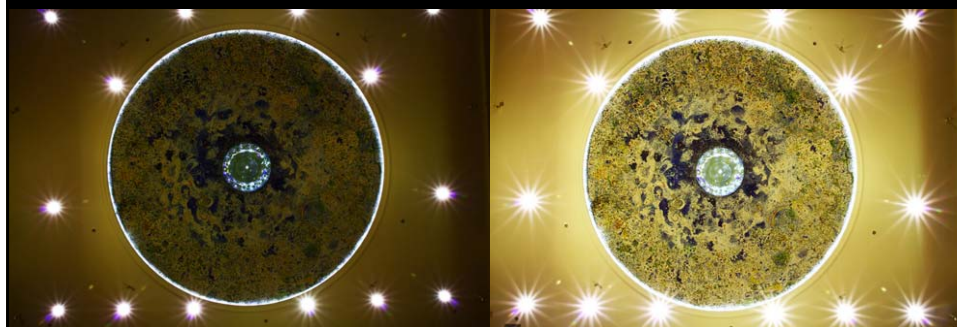
Avg. cost per patient per year



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Long acting risperidone (**New indication**)

(成大醫院/蒼穹之窗)

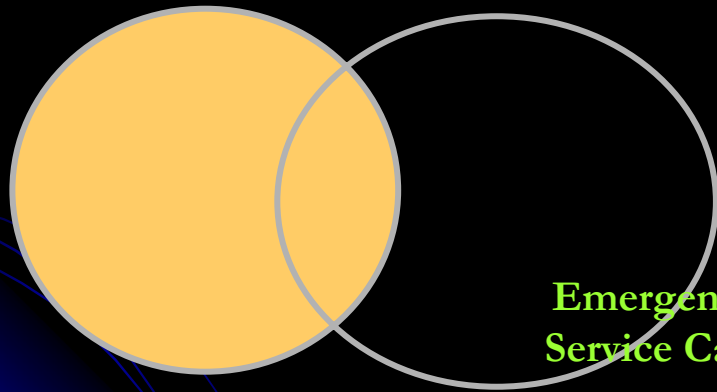


Subjects

at least one acute admission based upon principal diagnosis of BD (ICD-9-CM code: 296.0X, 296.1X, 296.4X, 296.5X, 296.6X, 296.7X, 296.80, or 296.89) between January 1, 2006 and December 31, 2006 (入院與出院日)

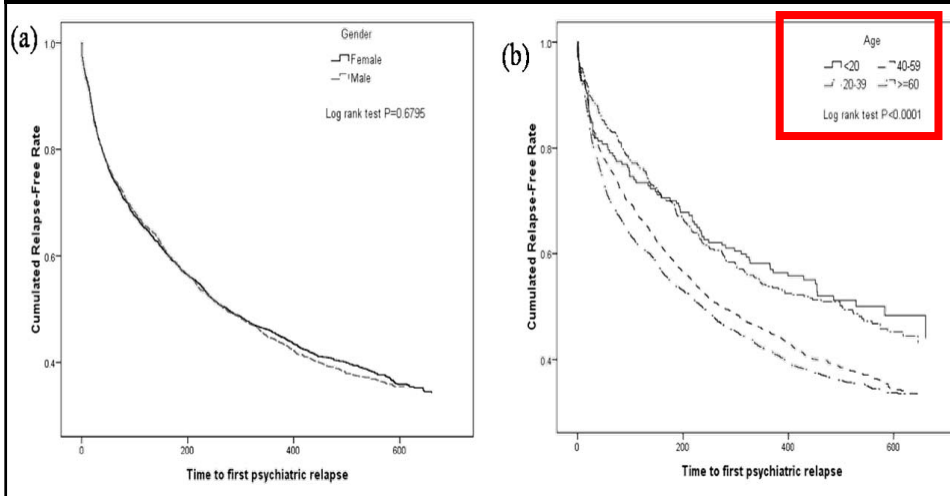
- if each admission occurring within 14 days of the discharge date of a previous one, the two events being regarded as one hospitalization episode.
- 4,267 cases for analysis in this study (4,401-134 loss of NHI beneficiary status)

Relapse vs. Rehospitalization

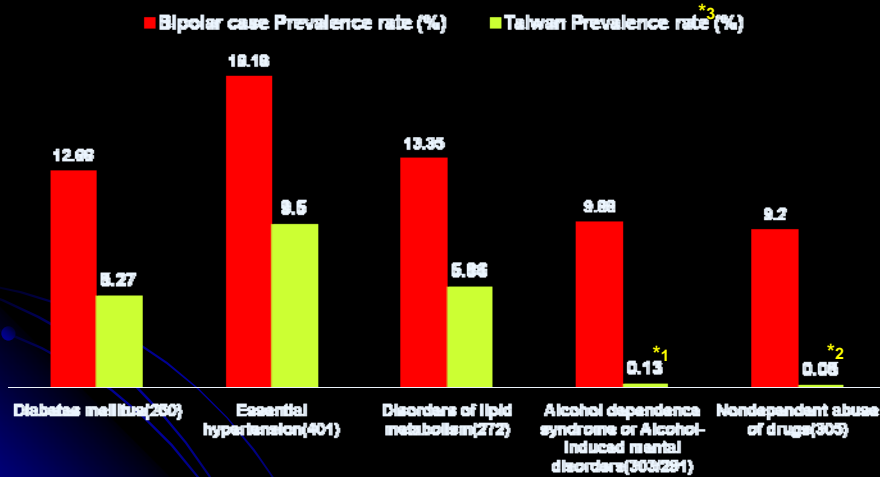


Emergency Service Care

Time to first relapse within 12 months of the index discharge (by gender and age group)



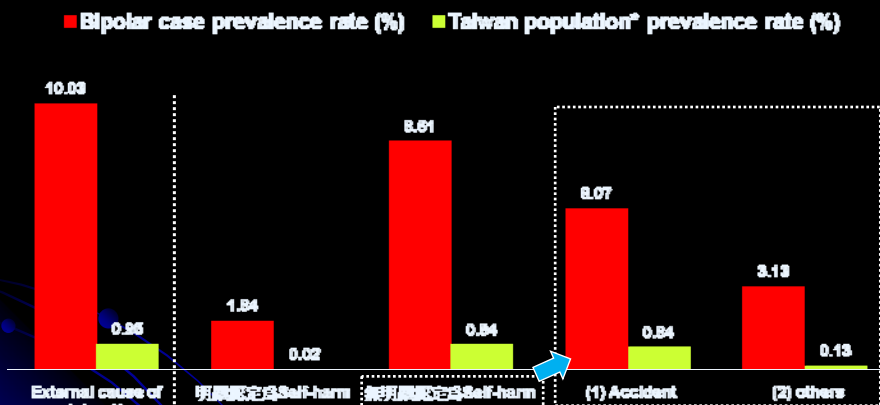
Co-morbidities Prevalence rate (Hsieh M Het al)



*1. Alcohol abuse (ICD9-CM:291+303+305.0)=0.21% (ICD9-CM:303)=0.13%
 *2. Drug abuse (ICD9-CM:304,305.2-305.9)=0.05%
 *3. Taiwan prevalence rate 資料來源:衛生署公告之2006年門、住診合計(包括急診)診診率

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Bipolar患者意外分佈情況及全國比較 (N=2,173) (Hsieh M Het al)



全國Prevalence rate: 國衛院發行之全民健保資料庫2006年住院醫療費用清單明確之該年住院人數/年中人口數

**本研究以B-code碼確定意外事件,分類如下:

1.Self-harm(明顯認定為Self-harm): 'B950', 'B956', 'B958', 'B959', 'B952', 'B957', 'B953', 'B951'
 2.Accident(無明顯認定為Self-harm): 'B885', 'B929', 'B860', 'B866', 'B917', 'B920', 'B884', 'B819', 'B968', 'B849', 'B853', 'B878', 'B852', 'B924', 'B812', 'B927', 'B816', 'B818', 'B988', 'B826', 'B858', 'B879', 'B880', 'B883', 'B906', 'B915', 'B989', 'B815', 'B854', 'B855', 'B876', 'B893', 'B898', 'B899', 'B905', 'B918', 'B969'
 3.Others(無明顯認定為Self-harm): 'B928', 'B939', 'B936', 'B980', 'B888', 'B947', 'B960', 'B887', 'B937', 'B931', 'B933', 'B943', 'B945'

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Conclusion

- Model selection
- Unit price for different treatment
- To estimate compliance rates
- To figure out different treatment rates
- Target population/duration
- Data selection/experts

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謝謝聆聽 (飛躍勝利/邁向成功)
Thanks for your attention!

