

# Evidence Based Medicine

Reporter : R3 陳昭松

Supervisor : VS 葉怡君



## Personal profile

- Name : Mrs. X
- Sex: female
- Age :81 year-old
- Marital status : married
- Education : illiteracy
- Occupation: joblessness
- Domicile : living with her families
- Referral from: OPD

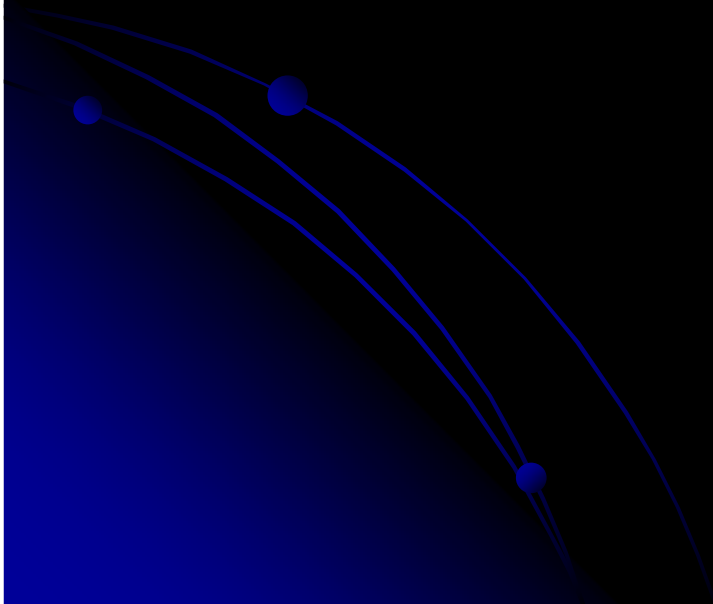
# Clinical Situation

- Chief complaint : agitation occasionally and irritable mood for several months.
- Present illness : This 81 year-old female patient is a case of dementia with BPSD ( behavioral and psychological symptoms of dementia ) with regular OPD follow-up.
- She suffered from irritable mood with occasionally agitated behavior for several months. Besides, poor sleep with restless was noted at night.
- Sometimes, multiple somatic complaint such as dizziness, headache and general weakness were also noted.
- Antipsychotic such as ziprasidone, paliperidone, aripiprazole and quetiapine were tried before but in vain

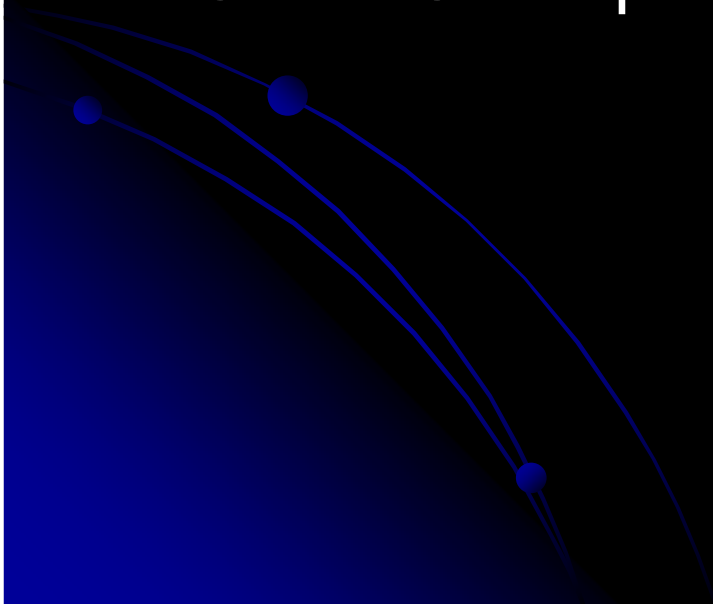
- Antipsychotic is effective to schizophrenia with psychosis and agitation, does it also effective to dementia with psychosis and agitation ?
- Previous doctors had tried some antipsychotics before such as ziprasidone, quetiapine, paliperidone and aripiprazole, may we try risperidone for further treatment? Is it evident-based?

- Step 1

- 形成臨床問題

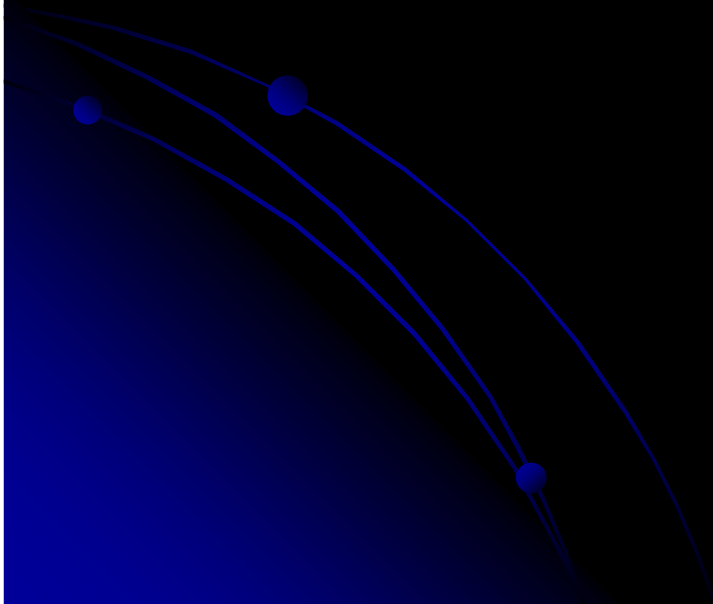


- P : dementia with BPSD ( behavioral and psychological symptoms of dementia )
- I : risperidone
- C : placebo
- O : BPSD improved



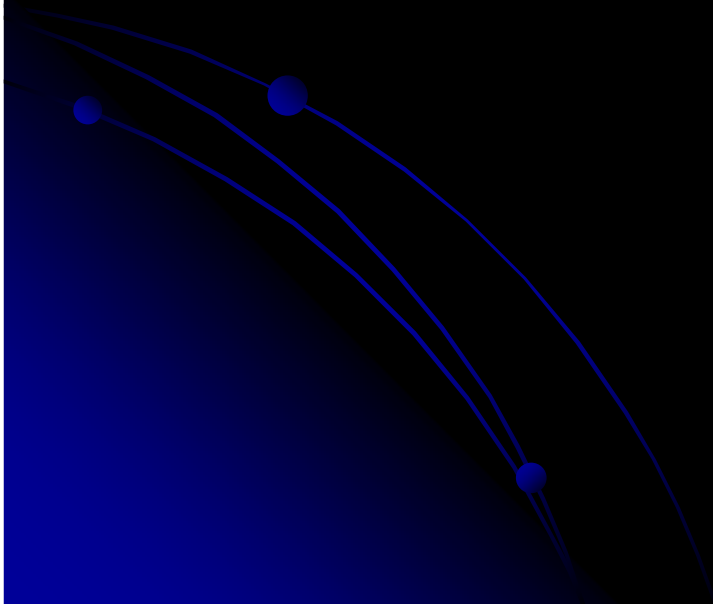
- Step 2

- 尋找證據



# Search strategy (1)

- Pub med
- Key word : dementia with BPSD ( behavioral and psychological symptoms of dementia ), risperidone



Windows Live search bar, navigation icons, and utility buttons.

PubMed.gov search interface with search bar containing "behavioral and psychological symptoms of dementia".

Display Settings: Summary, 20 per page, Sorted by Recently Added

Results: 1 to 20 of 1710

- 1. [Are the Behavioral Symptoms of Alzheimer's Disease Directly Associated with Neurodegeneration?](#)  
Serra L, Perri R, Cercignani M, Spanò B, Fadda L, Marra C, Carlesimo GA, Caltagirone C, Bozzali M.  
J Alzheimers Dis. 2010 Jun 16. [Epub ahead of print]  
PMID: 20555138 [PubMed - as supplied by publisher]  
[Related citations](#)
- 2. [Prevalence of psychiatric disorders among older adults in long-term care homes: a systematic review.](#)  
Seitz D, Purandare N, Conn D.  
Int Psychogeriatr. 2010 Jun 4:1-15. [Epub ahead of print]  
PMID: 20522279 [PubMed - as supplied by publisher]  
[Related citations](#)
- 3. [Drug Class Review: Atypical Antipsychotic Drugs: Final Report Update 2 \[Internet\].](#)  
McDonagh MS, Peterson K, Carson S, Chan B, Thakurta S  
Portland, (OR): Oregon Health & Science University; 2008 Jun.

Filter your results: All (1710), Review (295), Free Full Text (174)

Titles with your search terms: [Anticonvulsant mood stabilizers in the treatment of behavioral and p [Encephale. 2008], Behavioral and psychological symptoms of dementia and bipolar spectr [CNS Spectr. 2008], Lavender aroma therapy for behavioral and psychological sympt [Geriatr Gerontol Int. 2008]

risperidone - PubMed result - PCMan Combo

連線 (C) 編輯 (E) 選項 (V) BBS最愛 (B) Web最愛 (A) 紀錄 (Y) ANSI編輯 (N) 工具 (I) 說明 (H)

http://www.ncbi.nlm.nih.gov/sites/pubmed

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National Institutes of Health

Search: PubMed  
risperidone Search Clear

Display Settings: Summary, 20 per page, Sorted by Recently Added Send to:

**Results: 1 to 20 of 5752** << First < Prev Page 1 Next > Last >>

[Metabolic profile of first and second generation antipsychotics among Chinese patients.](#)  
1. Lee E, Chow LY, Leung CM.  
Psychiatry Res. 2010 May 27. [Epub ahead of print]  
PMID: 20554016 [PubMed - as supplied by publisher]  
[Related citations](#)

[Comparison of the metabolic and economic consequences of long-term treatment of schizophrenia using ziprasidone, olanzapine, quetiapine and risperidone in Canada: a cost-effectiveness analysis.](#)  
2. McIntyre RS, Cragin L, Sorensen S, Naci H, Baker T, Roussy JP.  
J Eval Clin Pract. 2010 Jun 10. [Epub ahead of print]  
PMID: 20545800 [PubMed - as supplied by publisher]  
[Related citations](#)

[Severe Extrapiramidal Symptoms After Nonintentional Risperidone Exposure in a Child: Case Report and Review of the Literature.](#)  
3. Glatstein M, Sulowski C, Waisburg C, Koren G, Garcia-Bourmissen F.  
Am J Ther. 2010 Jun 9. [Epub ahead of print]  
PMID: 20543664 [PubMed - as supplied by publisher]  
[Related citations](#)

[Effect of risperidone on acute methamphetamine-induced hyperthermia in rats.](#)  
4. Shioda K, Nishiima K, Yoshino T, Kato S

Filter your results:  
All (5752)  
[Review \(1015\)](#)  
[Free Full Text \(879\)](#)  
[Manage Filters](#)

Also try:  
risperidone schizophrenia  
risperidone children  
risperidone autism  
risperidone bipolar  
long acting risperidone

Titles with your search terms  
Use of long-acting risperidone in psychiatric disorders: focus or [Expert Rev Neurother. 2009]  
Amisulpride the 'atypical' atypical antipsychotic-comparison to haloperidol [Schizophr Res. 2008]

完成

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(risperidone) and (behavioral and psychological symptoms of dementia) - PubMed result - PCMan Combo

連線 (C) 編輯 (E) 選項 (V) BBS最愛 (B) Web最愛 (A) 紀錄 (Y) ANST編輯 (N) 工具 (T) 說明 (H)

http://www.ncbi.nlm.nih.gov/sites/pubmed

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Search: PubMed  
[risperidone) and (behavioral and psychological symptoms of dementia) Search Clear

Display Settings: Summary, 20 per page, Sorted by Recently Added

Results: 1 to 20 of 58

1. [Yokukansan inhibits social isolation-induced aggression and methamphetamine-induced hyperlocomotion in rodents.](#)  
Uchida N, Egashira N, Iwasaki K, Ishibashi A, Tashiro R, Nogami A, Manome N, Abe M, Takasaki K, Mishima K, Takata J, Oishi R, Nishimura R, Fujiwara M.  
Biol Pharm Bull. 2009 Mar;32(3):372-5.  
PMID: 19252280 [PubMed - indexed for MEDLINE] Free Article  
[Related citations](#)

2. [\[Recognition and treatment of behavioral and psychological symptoms of dementias: lessons from the CATIE-AD study\]](#)  
Kálmán J, Kálmán S, Pákási M.  
Neuropsychopharmacol Hung. 2008 Oct;10(4):233-49. Review. Hungarian.  
PMID: 19213202 [PubMed - indexed for MEDLINE]  
[Related citations](#)

3. [\[The use of antipsychotics in patients with dementia\]](#)  
Forlenza OV, Cretaz E, Diniz BS.  
Rev Bras Psiquiatr. 2008 Sep;30(3):265-70. Review. Portuguese.  
PMID: 18833428 [PubMed - indexed for MEDLINE] Free Article  
[Related citations](#)

4. [Risperidone, olanzapine and quetiapine in the treatment of behavioral and psychological symptoms in patients with Alzheimer's disease: preliminary findings from a naturalistic, retrospective study.](#)

Filter your results:  
All (58)  
[Review \(20\)](#)  
[Free Full Text \(6\)](#)  
[Manage Filters](#)

Titles with your search terms  
Behavioral and psychological symptoms in patients with dementia : [J Clin Psychiatry. 2004]  
Evaluation of risperidone in the treatment of behavioral and psycho [Int Psychogeriatr. 2005]  
Effects of risperidone on behavioral and psychological symptom [Int Psychogeriatr. 2005]  
See more...

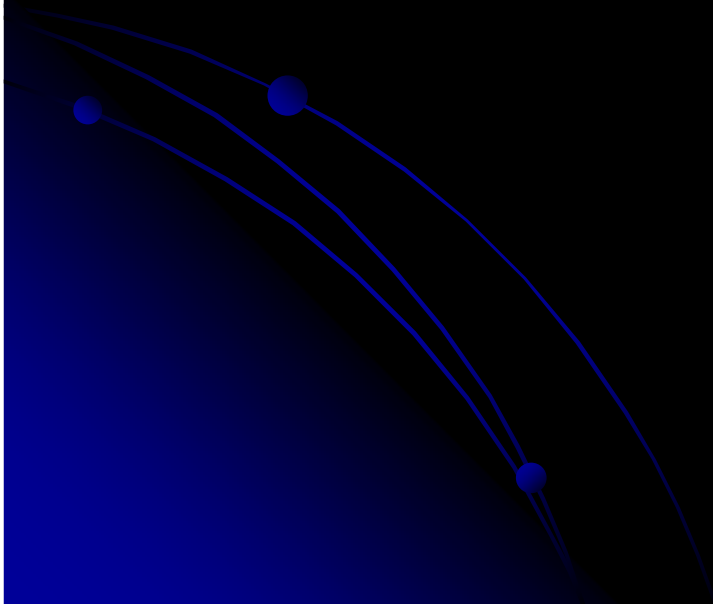
1 free full-text article in PubMed Central  
[Review](#) Atypical antipsychotic drugs in the treatment of behavioural and psych [BMJ. 2004]

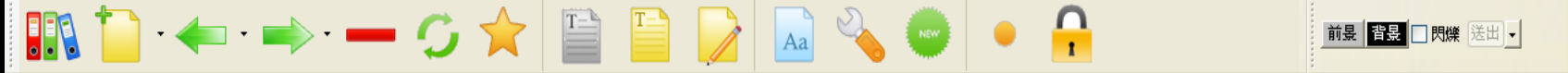
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## Search strategy (2)

- Limit : human, English, meta-analysis, randomized controlled trial





The following term was ignored: (

See the search details.

Limits Activated: Humans, Meta-Analysis, Randomized Controlled Trial, English [Change](#) | [Remove](#)

Results: 11

- [The efficacy and safety of risperidone in the treatment of psychosis of Alzheimer's disease and mixed dementia: a meta-analysis of 4 placebo-controlled clinical trials.](#)  
1. Katz I, de Deyn PP, Mintzer J, Greenspan A, Zhu Y, Brodaty H.  
Int J Geriatr Psychiatry. 2007 May;22(5):475-84.  
PMID: 17471598 [PubMed - indexed for MEDLINE]  
[Related citations](#)
- [Amisulpride versus risperidone treatment for behavioral and psychological symptoms in patients with dementia of the Alzheimer type: a randomized, open, prospective study.](#)  
2. Lim HK, Pae CU, Lee C, Lee CU.  
Neuropsychobiology. 2006;54(4):247-51. Epub 2007 Mar 15.  
PMID: 17356308 [PubMed - indexed for MEDLINE]  
[Related citations](#)
- [Mortality in elderly dementia patients treated with risperidone.](#)  
3. Haupt M, Cruz-Jentoft A, Jeste D.  
J Clin Psychopharmacol. 2006 Dec;26(6):566-70.  
PMID: 17110812 [PubMed - indexed for MEDLINE]  
[Related citations](#)
- [Treating behavioral and psychological symptoms in patients with psychosis of Alzheimer's disease using risperidone.](#)  
4. Rabinowitz J, Katz I, De Deyn PP, Greenspan A, Brodaty H.  
Int Psychogeriatr. 2007 Apr;19(2):227-40. Epub 2006 Jul 31.  
PMID: 16879763 [PubMed - indexed for MEDLINE]  
[Related citations](#)

Review (0)  
Free Full Text (0)  
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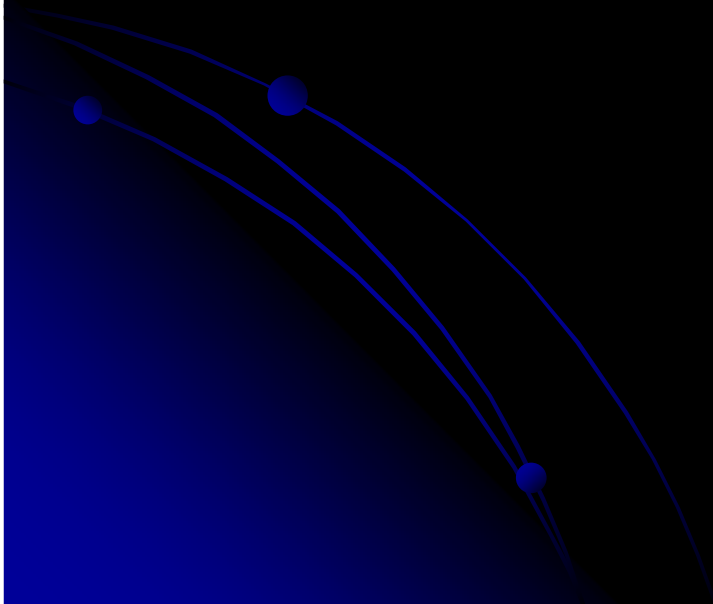
**Titles with your search terms**  
Evaluation of risperidone in the treatment of behavioral and psycho [Int Psychogeriatr. 2005]  
Clinical experience with risperidone in the [Prog Neuropsychopharmacol Biol Psychiatry. ...]  
Effects of risperidone on behavioral and psychological symptom [Int Psychogeriatr. 2005]  
[See more...](#)

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**Search details**  
("risperidone"[MeSH Terms]  
OR "risperidone"[All Fields])  
AND (("behavior"[MeSH Terms]  
OR "behavior"[All Fields])  
OR "behavioral"[All Fields])

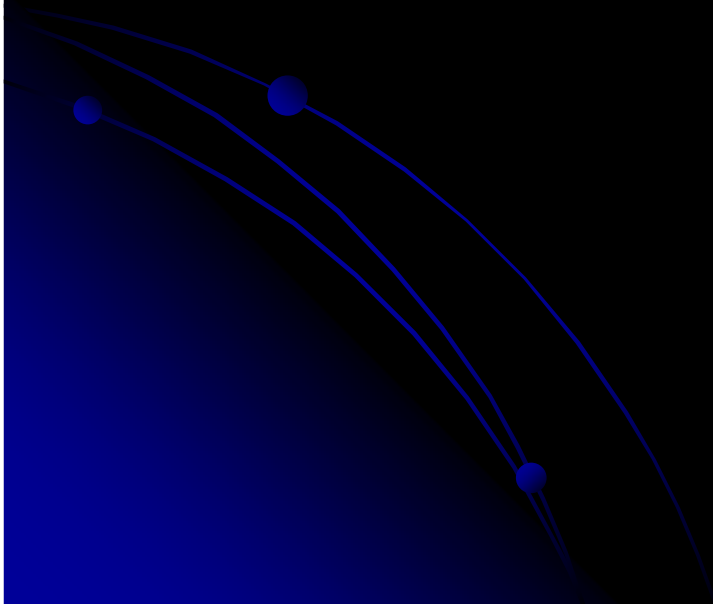
## Search strategy (3)

- 共11篇，找出與主題相關者共3篇



- Step 3 :

- 證據評估



# Evidence appraisal (1)

- The efficacy and safety of risperidone in the treatment of psychosis of Alzheimer's disease and mixed dementia: a meta-analysis of 4 placebo-controlled clinical trials
- Katz I, de Deyn PP, Mintzer J, Greenspan A, Zhu Y, Brodaty H.
- Int J Geriatr Psychiatry. 2007 May;22(5):475-84

- Patients with psychosis of AD from **four large placebo controlled clinical trials** of risperidone in dementia, meta-analysis.

## Evidence appraisal (2)

- Treating behavioral and psychological symptoms in patients with psychosis of Alzheimer's disease using risperidone
- Rabinowitz J, Katz I, De Deyn PP, Greenspan A, Brodaty H.
- Int Psychogeriatr. 2007 Apr;19(2):227-40. Epub 2006 Jul 31
- 479 nursing-home patients, three 12-week, **double-blind, placebo-controlled clinical trials**, rate with Cohen-Mansfield Agitation Inventory (CMAI) and BEHAVE-AD

## Evidence appraisal (3)

- Evaluation of risperidone in the treatment of behavioral and psychological symptoms and sleep disturbances associated with dementia.

- Durán JC, Greenspan A, Diago JI, Gallego R, Martinez G.

- Int Psychogeriatr. 2005 Dec;17(4):591-604. Epub 2005 Oct 5.

- 338 patients, 12-week, **observational, prospective study**, effects of risperidone were assessed using the Neuropsychiatric Inventory (NPI) total and subscale scores

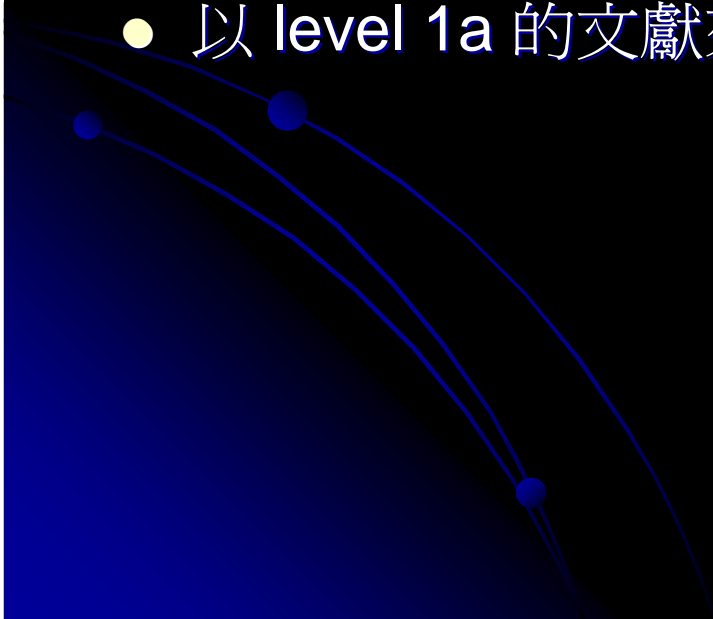
# 證據等級

Level	與[治療/預防/病因/危害]有關的文獻
1a	用多篇RCT所做成的綜合性分析(SR of RCTs)
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series (poor quality :cohort / case-control studies)
5	沒有經過完整評讀醫學文獻的專家意見

# 文獻證據等級應用

- Evidence appraisal (1) -- Level 1a
- Evidence appraisal (2) -- Level 1b
- Evidence appraisal (3) – Level 2b

- 以 level 1a 的文獻來做佐證

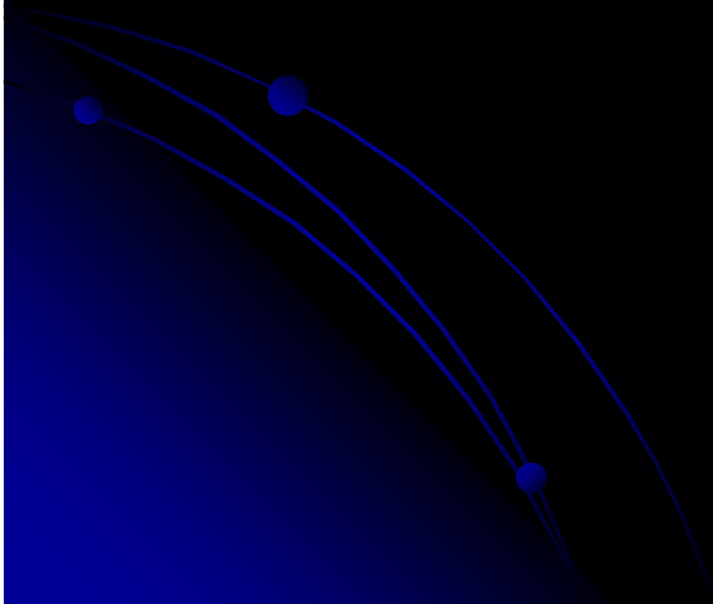


- The efficacy and safety of risperidone in the treatment of psychosis of Alzheimer's disease and mixed dementia: a meta-analysis of 4 placebo-controlled clinical trials
- METHODS: This study is a meta-analysis of patients with psychosis of AD from four large placebo-controlled clinical trials of risperidone in dementia. Three trials included patients diagnosed with heterogeneous symptoms of BPSD (those with psychosis of AD were included in this analysis), while one trial included only those diagnosed with psychosis of AD. Efficacy was measured using the Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) Psychosis subscale and Clinical Global Impression (CGI).

- **RESULTS:** Primary analyses in the psychosis of AD population demonstrated that risperidone significantly improved scores on the BEHAVE-AD Psychosis subscale and CGI scale compared with placebo. Secondary analyses demonstrated that patients with more severe symptoms showed a more pronounced response to treatment with risperidone compared with placebo than those patients with less severe symptoms. Extrapyramidal symptoms and somnolence were more frequent with risperidone than placebo ( $p=0.04$ ). Cerebrovascular adverse events and all-cause mortality were observed more frequently, although not statistically significantly, with risperidone versus placebo.
- **CONCLUSIONS:** This meta-analysis of psychosis of AD showed **improvement in psychotic symptoms and general clinical improvement in patients with psychosis of AD treated with risperidone compared with placebo.** The benefits of treatment were most significant in patients with severe symptoms. **The safety profile of risperidone in this psychosis of AD population was similar to the more general BPSD population**

- Step 4

- 臨床應用



## Plain-language explanation

- 可跟Mr. X 的家屬解釋目前Mr. X的情形是由於Alzheimer's disease引起的精神和行為問題，包括情緒和睡眠方面的干擾。針對這部份，已有一些研究顯示抗精神病藥risperidone對於這部份有顯著的療效，所以可以考慮用這藥物來做進一步的治療。當然在使用藥物的同時也必須告知病患及家屬藥物可能有的副作用。

# Serious AE (CVA) of Antipsychotics in Dementia

- Meta-analysis of pooled data (totally 3327 patients on antipsychotics and 1728 on placebo) showed increased cerebrovascular events in antipsychotics (Risperidone, Olanzapine, Aripiprazole, Quetiapine). (OR=2.13, p=0.009)
  - Significantly increased risk with risperidone (OR=3.43)
- FDA warning of stroke risks for use of antipsychotics
  - Risperidone in April, 2003
  - Olanzapine in Jan, 2004
  - Aripiprazole in Feb, 2005
  - Clozapine, Ziprasidone, Symbyax in April, 2005

<http://www.fda.gov/cder/drug/advisory/antipsychotics.htm>