實證醫學簡介及臨床應用

銀杏預防老人癡呆?

主講人:林美吟藥師

日期:99.7.23(五)

Problem description(臨床問題敘述)

- 王老太太，今年75歲，最近常常發現忘記東西放在怎麼地方、上菜市場買菜常記不得買的東西多少錢、記憶力不好而且注意力也不佳 ，女兒擔心媽媽有失智的情形，因此請教隔壁的張媽媽，張媽媽介紹可以吃銀杏來預防老人癡呆症。王老太太的女兒懷疑是否真的有效?希望醫師能給予推薦。

將問題寫成PICO

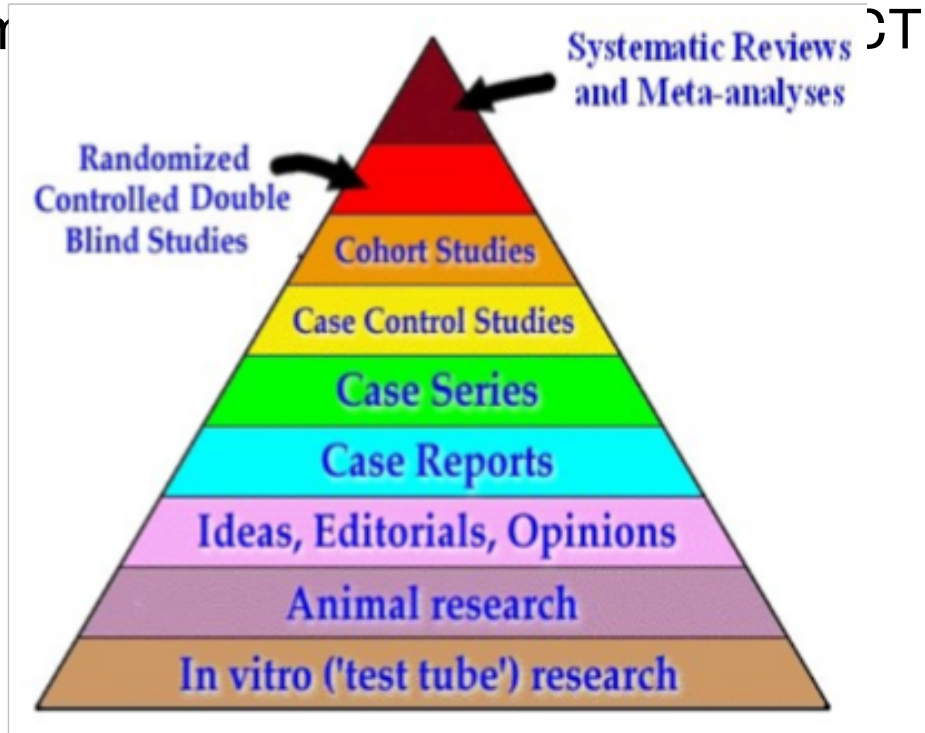
問題類型	■治療性 □診斷性 □預後性 □併發性	
	中文	英文
P	Normal cognition or mild cognitive impairment patients	正常認知功能或輕度認知功能不良的老人
I	Ginkgo biloba	銀杏
C	Placebo	安慰組
O	Prevention dementia	預防老人癡呆症

Key words(關鍵字)設定

	主要詞彙(Primary Term)
P	Normal cognition, mild cognitive impairment
I **C**	Ginkgo biloba, EGB 761
O	Prevention, dementia, Alzheimer disease

資料庫搜尋策略

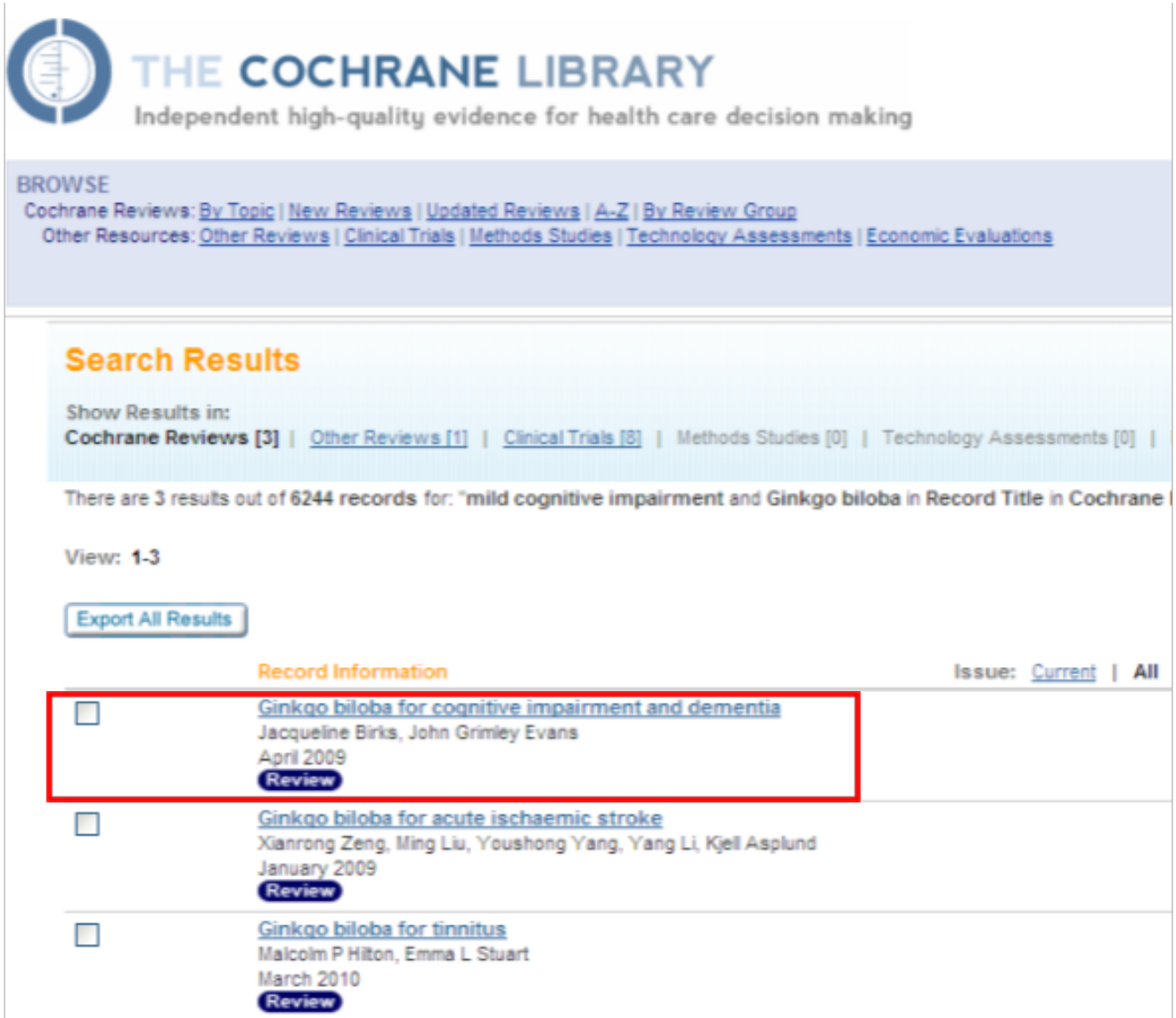
- 搜尋策略
  - Primary Database
    - PubMed
  - Secondary Database
    - Cochrane Library、UpToDate
  - Study Design
    - Systen CT



THE COCHRANE LIBRARY
Independent high-quality evidence for health care decision making

搜尋cochrane library

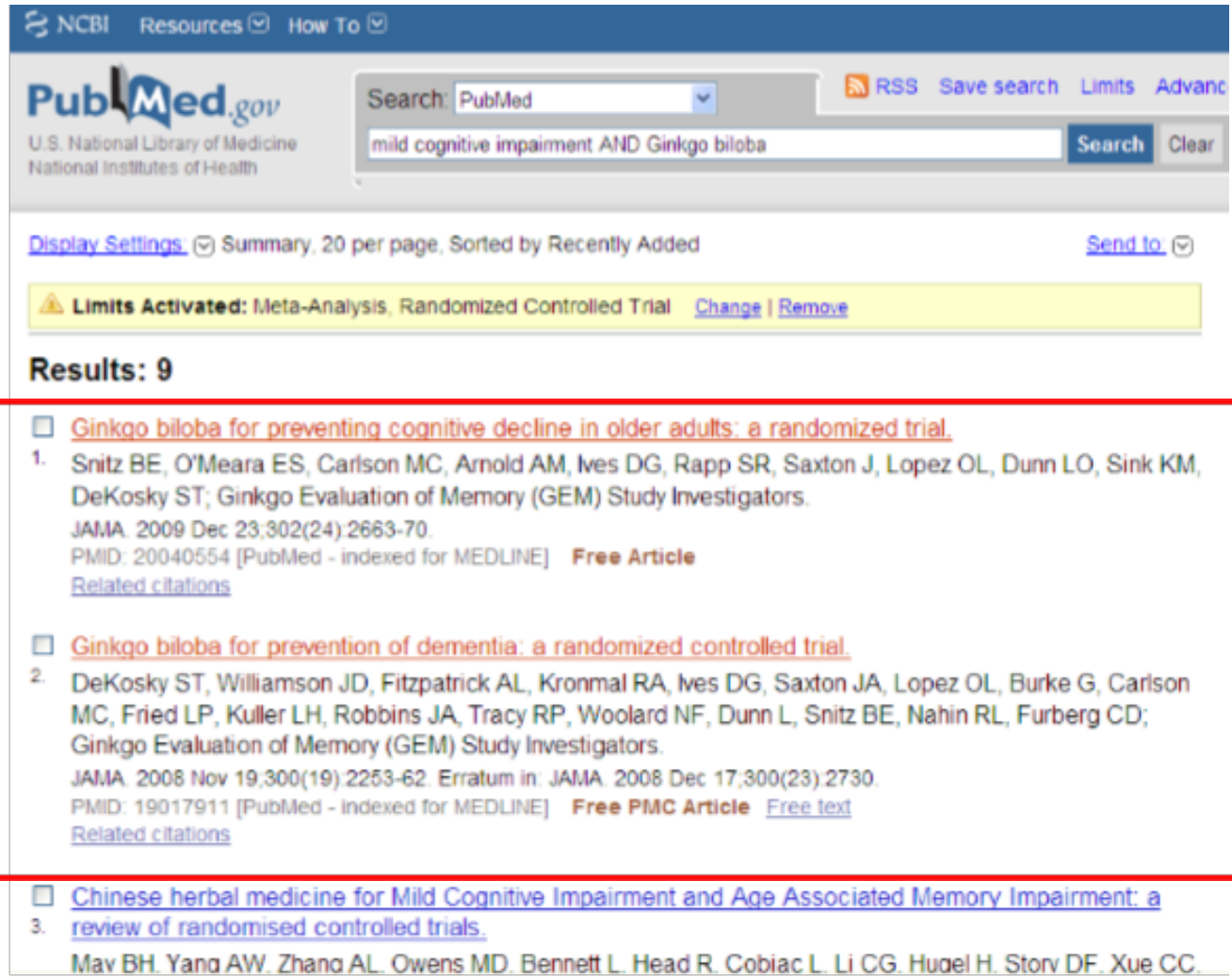
- 關鍵字：mild cognitive impairment AND Ginkgo biloba



PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

搜尋PubMed

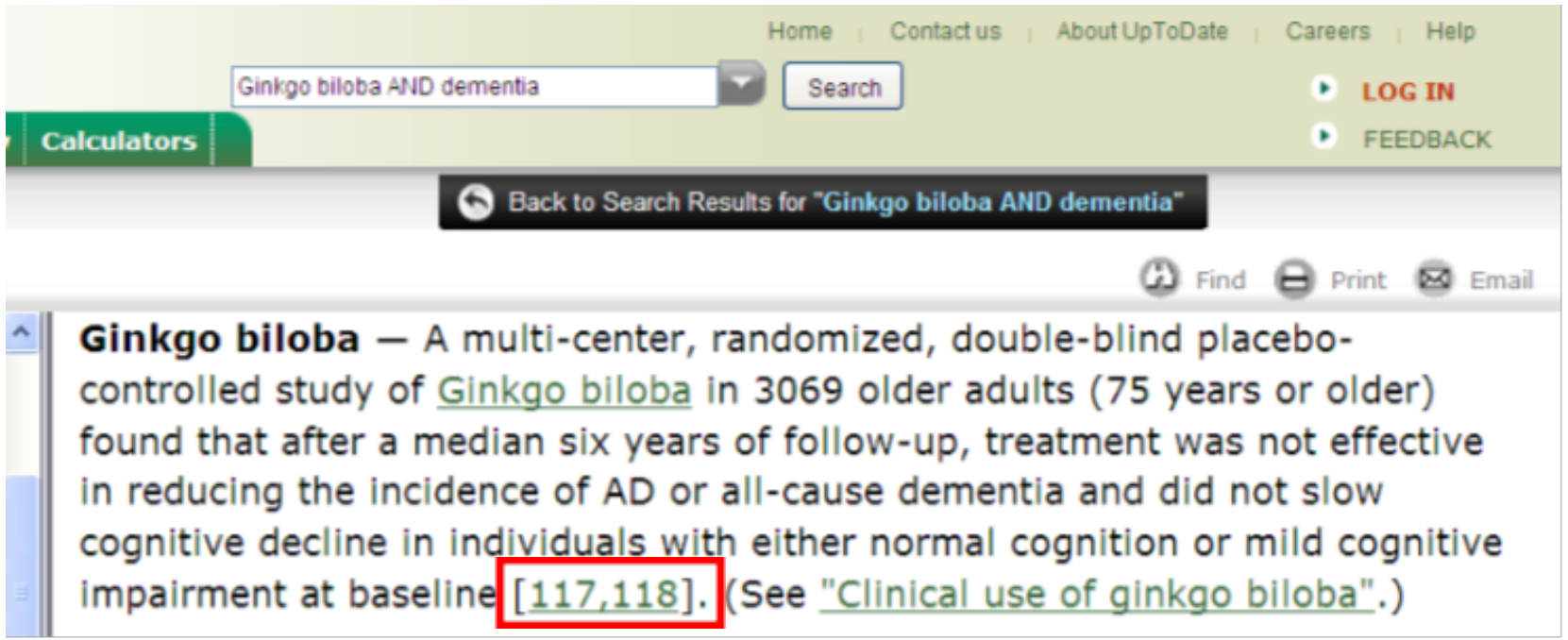
- 關鍵字：mild cognitive impairment AND Ginkgo biloba



UpToDate ONLINE 18.1

搜尋UpToDate

- 關鍵字：Ginkgo biloba AND dementia



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TI Ginkgo biloba for Prevention of Dementia: A Randomized Controlled Trial.

AU Dekosky ST; Williamson JD; Fitzpatrick AL; Kronmal RA; Ives DG; Saxton JA; Lopez OL; Burke G; Carlson MC; Fried LP; Kuller LH; Robbins JA; Tracy RP; Woolard NF; Dunn L; Snitz BE; Nahin RL; Furberg CD

SO JAMA. 2008 Nov 19;300(19):2253-2262.

118

TI Ginkgo biloba for preventing cognitive decline in older adults: a randomized trial.

AU Snitz BE; O'Meara ES; Carlson MC; Arnold AM; Ives DG; Rapp SR; Saxton J; Lopez OL; Dunn LO; Sink KM; DeKosky ST

SO JAMA. 2009 Dec 23;302(24):2663-70.

資料庫搜尋結果

資料庫種類	文章篇數	不符合	符合
UpToDate. ONLINE 18.1	2	0	2
THE COCHRANE LIBRARY Independent high-quality evidence for health care decision making	3	2	1
PubMed.gov U.S. National Library of Medicine National Institutes of Health	9	7	2

1.系統回溯性的文獻

[Intervention Review]

Ginkgo biloba for cognitive impairment and dementia

Jacqueline Birks[1], John Grimley Evans[2]

[1]Centre for Statistics in Medicine, University of Oxford, Oxford, UK. [2]Division of Clinical Geratology, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK

Contact address: Jacqueline Birks, Centre for Statistics in Medicine, University of Oxford, Wolfson College, Linton Road, Oxford, OX2 6UD, UK. jacqueline.birks@csm.ox.ac.uk.

Editorial group: Cochrane Dementia and Cognitive Improvement Group.
Publication status and date: Edited (no change to conclusions), published in Issue 2, 2009.
Review content assessed as up-to-date: 25 March 2008.

2.RCT治療性的文獻

JAMA®

Online article and related content current as of June 30, 2010.

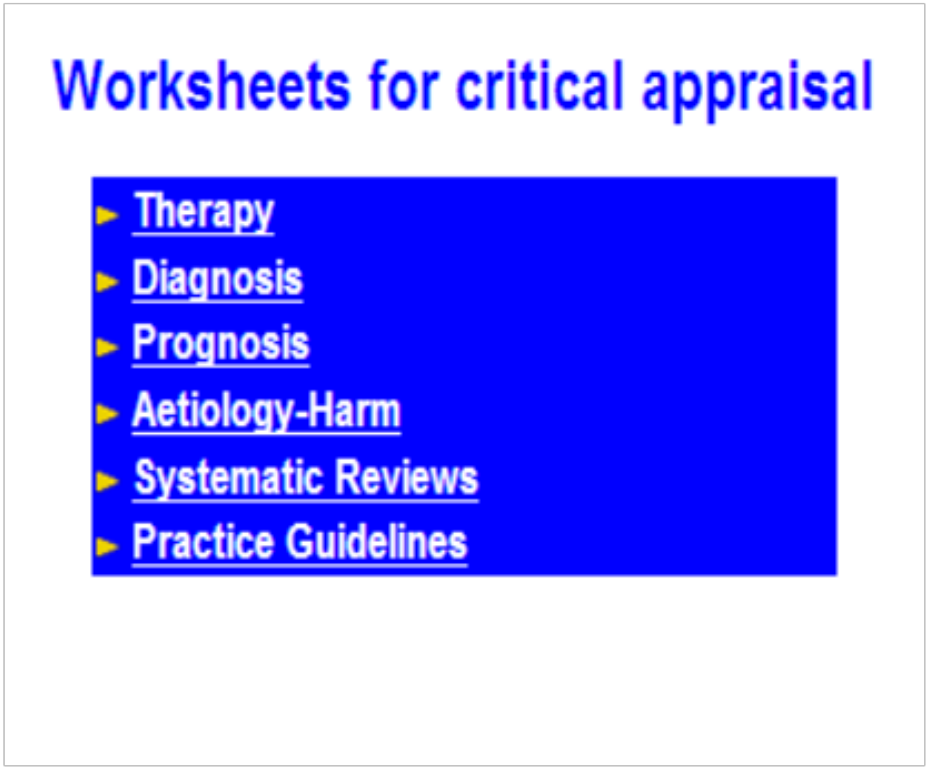
Ginkgo biloba for Prevention of Dementia: A Randomized Controlled Trial

Steven T. DeKosky; Jeff D. Williamson; Annette L. Fitzpatrick; et al.

JAMA. 2008;300(19):2253-2262 (doi:10.1001/jama.2008.683)

文獻評讀工具

- Oxford levels of evidence
- Worksheets for critical appraisal (CEFPAS)



1.系統回溯性的文獻

系統回溯性的文獻評讀內容

- Validity/Reliability (效度/信度)
- Importance/Impact (重要性)
- Practice/Applicability (臨床適用性)

[Intervention Review]

Ginkgo biloba for cognitive impairment and dementia

Jacqueline Birks[1], John Grimley Evans[2]

[1]Centre for Statistics in Medicine, University of Oxford, Oxford, UK. [2]Division of Clinical Geratology, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK

Contact address: Jacqueline Birks, Centre for Statistics in Medicine, University of Oxford, Wolfson College, Linton Road, Oxford, OX2 6UD, UK. jacqueline.birks@csm.ox.ac.uk.

Editorial group: Cochrane Dementia and Cognitive Improvement Group.
Publication status and date: Edited (no change to conclusions), published in Issue 2, 2009.
Review content assessed as up-to-date: 25 March 2008.

Are the results of this systematic review valid?

Consider	Comment	
1.Is this a systematic review of randomised trials?	**METHODS** **Criteria for considering studies for this review** **Types of studies** All relevant, unconfounded, randomized, double-blind placebo-controlled studies.	□是 □否 □不清楚
2. Does it include a methods section that describes: (a) finding and including all relevant trials? (b) assessing their individual validity?	**Search methods for identification of studies** The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG) was searched on 20 September 2007 for all years up to December 2005. This register contains records from the following major healthcare databases *The Cochrane Library*, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS, and many ongoing trial databases and other grey literature sources. The following search terms were used: ginkgo* or gingko* or tanakan or EGB761 or "EGB 761" or EGB-761. *The Cochrane Library*, MEDLINE, EMBASE, PsycINFO and 特別說明搜尋的過程與方法	□是 □否 □不清楚

Are the results of this systematic review valid?

Consider	Comment	
3. Were the results consistent from study to study?	**Objectives** 目的 To assess the efficacy and safety of Ginkgo biloba for dementia or cognitive decline. **AUTHORS' CONCLUSIONS** **Implications for practice** 作者的結論 Ginkgo biloba appears to be safe in use with no excess adverse effects compared with placebo. The evidence that Ginkgo biloba has predictable and clinically significant benefit for people with dementia or cognitive impairment is inconsistent and unreliable.	□是 □否 □不清楚
4. Were the individual patient data used in the analysis (or aggregate data)?	**Subgroup analyses** 次族群分析 A secondary objective, as stated in the protocol for the review, was that diagnostic subgroups would be examined if possible. When the first version of the review was written very few of the included trials identified the cause of the dementia or memory loss of the patients. The more recent trials include the diagnoses, and the	□是 □否 □不清楚

證據等級評估

Level		Therapy/Prevention, Aetiology/Harm
1	a	將隨機對照臨床試驗研究(RCT)以系統性評論後(systematic review: SR)的結果
	b	具有嚴格的信賴區間的個別
	c	無論使用何種研究方 ,完全正面,完全負面或完全無效的研究報告
2	a	將同質性的世代研 性評論後的結果
	b	個別世代研究 低於80%follow-up)
	c	以多數結果為基礎 研究
3	a	將同質性的個案對照 (case control studies),以系統性評論後的結果
	b	個別的個案對照研究(individual case control study)
4		病例統計報告,以及質量不足的個案對照研究
5		未經嚴謹評估的專家意見或基礎生理學,一般實驗室研究

Level 1a

英國的Oxford Centre證據應用等級

Are the valid results of this systematic review important?

治療24~26週後整體的功能(CGIC量表)表現

Analysis 1.7. Comparison 1 Ginkgo biloba vs placebo, Outcome 7 Global (CGIC) (numbers improved or unchanged compared with baseline) after treatment of 24-26 weeks.

Review: Ginkgo biloba for cognitive impairment and dementia

Comparison: 1 Ginkgo biloba vs placebo

Outcome: 7 Global (CGIC) (numbers improved or unchanged compared with

銀杏每天劑量<200mg

Study or subgroup	Ginkgo n/N	Placebo n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Ginkgo biloba dose less than 200mg/day special extract					
Le Bars 1997	98/154	94/155		46.2 %	1.14 [0.72, 1.80]
Schneider 2005	100/169	90/174		53.8 %	1.35 [0.88, 2.07]
Subtotal (95% CI)	**323**	**329**		**100.0 %**	**1.25 [0.91, 1.70]**
Total events: 198 (Ginkgo), 184 (Placebo)					
Heterogeneity: Chi² = 0.30, df = 1 (P = 0.59); I² =0.0%					
Test for overall effect: Z = 1.38 (P = 0.17)					
2 Ginkgo biloba dose greater than 200mg/day special extract					
Kanowski 1996	103/106	83/99		16.9 %	4.84 [1.89, 12.43]
Schneider 2005	104/170	90/174		83.1 %	1.47 [0.96, 2.25]
Subtotal (95% CI)	**276**	**273**		**100.0 %**	**1.80 [1.22, 2.65]**
Total events: 207 (Ginkgo), 173 (Placebo)					
Heterogeneity: Chi² = 5.13, df = 1 (P = 0.02); I² =80%					
Test for overall effect: Z = 2.96 (P = 0.0031)					
Test for subgroup differences: Chi² = 2.07, df = 1 (P = 0.1					

銀杏每天劑量>200mg

I^2=80%
1.異質性很高
2.樣本很少

OR=1.80,(95CI% 1.22-2.46) P=0.02

0.01 0.1 1 10 100

Favours placebo Favours Ginkgo

治療<12週，認知功能的表現

Analysis 1.10. Comparison 1 Ginkgo biloba vs placebo, Outcome 10 Cognition (change from baseline after treatment of less than 12 weeks).

Review: Ginkgo biloba for cognitive impairment and dementia

Comparison: 1 Ginkgo biloba vs placebo

Outcome: 10 Cognition (change from baseline after treatment of less than

銀杏每天劑量<200mg

P<0.05, 但是存在很高的異質性(I^2=92%)

Study or subgroup	Ginkgo N	Mean(SD)	Placebo N	Mean(SD)	Weight	Mean Difference
1 Ginkgo biloba dose less than 200mg/day special extract						
Brautigam 1998	130	-21.39 (2.45)	67	-21.38 (2.78)	30.8 %	0.00 [-0.30, 0.29]
Graessel 1992	28	-2.2 (24.6)	20	0.2 (23.4)	25.5 %	-0.10 [-0.67, 0.48]
Hofferberth 1989	18	-38.4 (13.1)	18	11.8 (14.7)	16.1 %	-3.53 [-4.61, -2.44]
Mancini 1993	34	-0.8 (5.6)	36	0.6 (5.33)	27.6 %	-0.25 [-0.72, 0.22]
Subtotal (95% CI)	**210**		**141**		**100.0 %**	**-0.81 [-1.73, 0.11]**

Heterogeneity: Tau^2 = 0.78; Chi^2 = 38.08, df = 3 (P<0.00001); I^2 =92%

Test for overall effect: Z = 1.73 (P = 0.084)

銀杏每天劑量<200mg
(排除Hofferberth et al.)

2 Ginkgo biloba dose less than 200mg/day special extract (Hofferberth omitted)						
Brautigam 1998	130	-21.39 (2.45)	67	-21.38 (2.78)	30.4 %	-0.10 [-0.67, 0.48]
Graessel 1992	28	-2.2 (24.6)	20	0.2 (23.4)	32.9 %	-0.25 [-0.72, 0.22]
Mancini 1993	34	-0.8 (5.6)	36	0.6 (5.33)	**100.0 %**	**-0.08 [-0.31, 0.15]**
Subtotal (95% CI)	**192**		**123**			

Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.78, df = 2 (P = 0.68); I^2 =0.0%

Test for overall effect: Z = 0.67 (P = 0.50)

沒有統計上的顯著差異

Favours Ginkgo Favours placebo

治療>12週，認知功能的表現

早期研究
樣本數很少
異質性很高

銀杏任何劑量
P=0.077
沒有統計意義

Analysis 1.27. Comparison 1 Ginkgo biloba vs placebo, Outcome 27 Number of patients experiencing an adverse event during treatment of 24-26 weeks.

治療>24週，副作用的評估

Review: Ginkgo biloba for cognitive impairment and dementia

Comparison: 1 Ginkgo biloba vs placebo

Outcome: 27 Number of patients experiencing an adverse event during treatment of 24-26 weeks

Study or subgroup	Ginkgo n/N	Placebo n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
1 Ginkgo biloba dose less than 200mg/day special extract				
DIGGER 2008	28/88	29/88		0.95 [0.50, 1.79]
Graessel 1992	4/36	6/36		0.63 [0.16, 2.43]
Le Bars 1997	43/166	44/161		0.93 [0.57, 1.52]
Mazza 2006	0/25	0/26		0.0 [0.0, 0.0]
Schneider 2005	114/169	124/174		0.84 [0.53, 1.32]
Subtotal (95% CI)	**484**	**485**		**0.88 [0.66, 1.17]**
Total events: 189 (Ginkgo), 203 (Placebo)				
Heterogeneity: Chi^2 = 0.40, df = 3 (P = 0.94); I^2 =0.0%				
Test for overall effect: Z = 0.87 (P = 0.38)				
2 Ginkgo biloba dose greater than 200mg/day special extract				
Napryeyenko 2005	166/200	178/200		0.60 [0.34, 1.07]
Schneider 2005	112/170	124/174		0.78 [0.49, 1.23]
Subtotal (95% CI)	**370**	**374**		**0.71 [0.49, 1.01]**
Total events: 278 (Ginkgo), 302 (Placebo)				
Heterogeneity: Chi^2 = 0.46, df = 1 (P = 0.50); I^2 =0.0%				
Test for overall effect: Z = 1.92 (P = 0.055)				

銀杏每天劑量>200mg
P=0.055 沒有統計意義

0.1 0.2 0.5 1 2 5 10

Favours Ginkgo Favours placebo

作者的結論

Authors' conclusions

Ginkgo biloba appears to be safe in use with no excess side effects compared with placebo. Many of the early trials used unsatisfactory methods, were small, and publication bias cannot be excluded. The evidence that Ginkgo biloba has predictable and clinically significant benefit for people with dementia or cognitive impairment is inconsistent and unreliable.

1. 服用銀杏安全性很高。
2. 早期研究受限於研究設計、試驗期間太短、以及沒有足夠的受試者參與、以致於無法證實銀杏在臨床上具有顯著治療效果。

2.RCT治療性的文獻

治療性的文獻評讀內容

- Validity/Reliability (效度/信度)
- Importance/Impact (重要性)
- Practice/Applicability (臨床適用性)

Ginkgo biloba for Prevention of Dementia
A Randomized Controlled Trial

研究目的
針對75歲以上，正常或是輕微認知障礙的老年人，
探討銀杏是否具有預防或延緩老人癡呆的療效

Lewis H. Kuller, MD, DrPH
John A. Robbins, MD, MHS
Russell P. Tracy, PhD
Nancy F. Woolard
Leslie Dunn, MPH
Beth E. Snitz, PhD
Richard L. Nahin, PhD, MPH
Curt D. Furberg, MD, PhD
for the Ginkgo Evaluation of Memory (GEM) Study Investigators

(n=1524).

Main Outcome Measures Incident dementia and AD determined by expert panel consensus.

The Ginkgo Evaluation of Memory Study
銀杏增強記憶評估研究

receiving
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person-

cebo group. The hazard ratio (HR) for *G biloba* compared with placebo for all-cause dementia was 1.12 (95% confidence interval [CI], 0.94-1.33; *P*=.21) and for AD, 1.16 (95% CI, 0.97-1.39; *P*=.11). *G biloba* also had no effect on the rate of progression to dementia in participants with MCI (HR, 1.13; 95% CI, 0.85-1.50; *P*=.39).

THE PREVENTION OF DISABLING

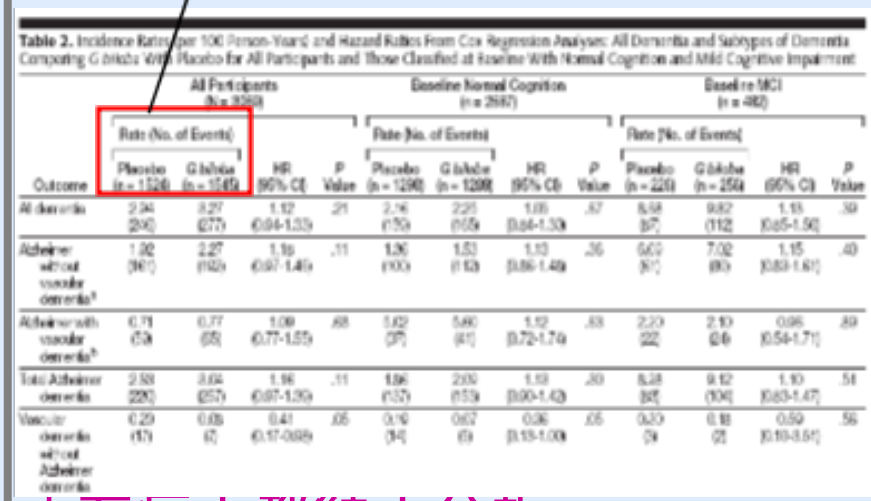
Are the results of this preventive or therapeutic trial valid?

塊狀排列隨機分派

Consider	Comment	
1.Was the assignment of patients to treatment randomised? Was the randomisation list concealed? 是否隨機分配病人至治療組?隨機是否有保密?	**Randomization** Assignment to *G biloba* or placebo was determined by permuted block design by site to ensure that allocation between treatment groups was well balanced. Randomization was done separately for each clinical site using a computer-generated, randomly permuted list maintained at the data coordinating center at the University of 文獻中很清楚提到randomization的詳細過程	□是 □否 □不清楚
2. Was follow-up of patients sufficiently long and complete? 病人追蹤期間是否夠長及完整?	**Design, Setting, and Participants** Randomized, double-blind, placebo-controlled clinical trial conducted in 5 academic medical centers in the United States between 2000 and 2008 with a median follow-up of 6.1 years. Three thousand sixty-nine community volunteers aged 75 years or older with normal cognition (n=2587) or MCI (n=482) at study entry were assessed every 6 months for incident dementia. 試驗期間長達8年(2000~2008)，平均追蹤6.1年，受試者3069人	□是 □否 □不清楚

Are the results of this preventive or therapeutic trial valid?

安慰組n=1524; 實驗組n=1549

Consider	Comment	
3. Where all patients analysed in the groups to which they were randomized? 納入研究的所有病人是否都有在結論中討論?是否都有在隨機時所分配的組別中分析?	 所有病人都納入分析	□是 □否 □不清楚
4. Were patients and clinicians keep “blind” to treatment? 病人及醫師是否皆對接受的治療遮盲?	used throughout the study. All clinical center and coordinating center personnel and participants were blinded to treatment assignment for the duration of the study. Only the study phar- 所有醫療機構及受試者皆blind只有參與的醫師及少數資料處理員知情	□是 □否 □不清楚

Are the results of this preventive or therapeutic trial valid?

Consider	Comment	
5. Were the groups treated equally, apart from the experimental treatment? 除了實驗性的治療外，各組間的其他處置是否相同?	**Study Intervention** Participants were randomized to twice-daily doses of either 120-mg *G biloba* extract (EGb 761; Schwabe Pharmaceuticals, Karlsruhe, Germany) or an identically appearing placebo. The formulation EGb 761 is 實驗組給予120mg 銀杏萃取物 (EGb 761) 其他處置相同，6個月追蹤一次	□是 □否 □不清楚
6.Were the groups similar at the start of the trial? 各組在研究開始時是否類似?	**Table 1.** Baseline Characteristics of Study Participants by Study Drug Assignment (*Ginkgo biloba* vs Placebo) No. (%) Characteristic / Placebo (n = 1524) / Ginkgo (n = 1545) / *P* Value Age, mean (SD), y: 79.1 (3.3) / 79.1 (3.3) / .88 Sex Female: 716 (47) / 702 (45) / .39 Male: 808 (53) / 843 (55) Race White: 1446 (95) / 1482 (96) / .23 Nonwhite: 76 (5) / 63 (4) Education High school or less: 534 (35) / 570 (37) / .40 Some college: 395 (26) / 380 (25) College graduate: 229 (15) / 250 (16) Postgraduate: 366 (24) / 344 (22) 兩組人口學及控制變項無顯著差異，顯示具平衡性。	□是 □否 □不清楚

Quality assessment for RCTs

- **Jadad Quality score文獻品質評量**

Item	score		
Was the study described as randomized (this includes such words as “randomly”, “random”,”randomization”)?	0/1	1	
was the method used to generate the sequence of randomization described and was it appropriate (eq. table of random numbers, computer-generated)?	0/1	1	
Was the study described as double-blind?	0/1	1	5
Was the method of double-blinding described and was it appropriate (eq. identical placebo, active placebo, dummy)	0/1	1	
Was there a description of withdrawals and dropouts?	0/1	1	
Deduct 1 point if the method used to generate the sequence of randomization was described but was inappropriate.	0/-1	0	
Deduct 1 point if the study was described as double-blind but the method of blinding was inappropriate.	0/-1	0	

Validity/Reliability

- 針對效度檢測的上述六個問題，答案均為肯定的，以及Jadad score≧3，故應是一篇值得參考的文獻。

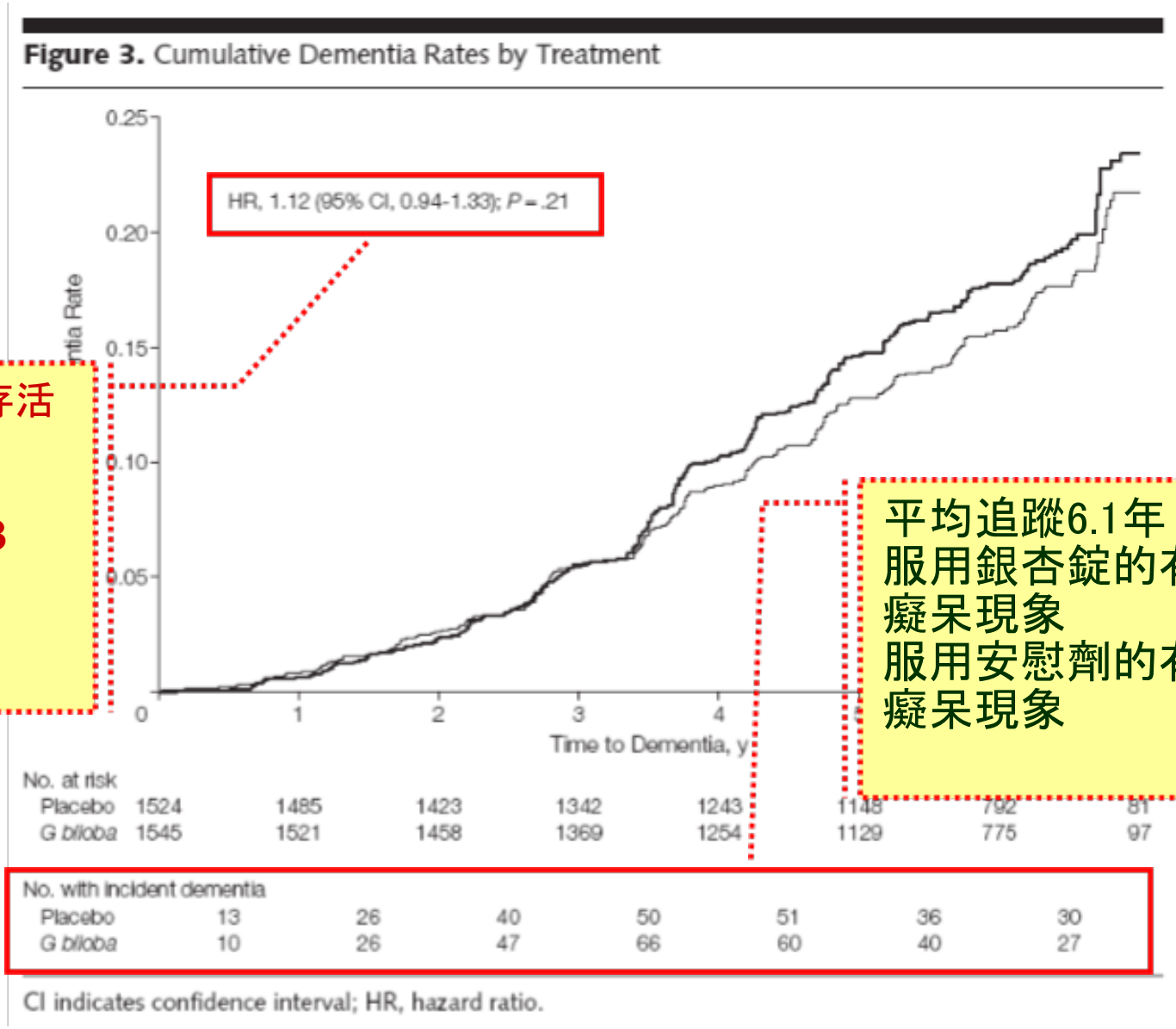
證據等級評估

Level		Therapy/Prevention, Aetiology/Harm
1	a	將隨機對照臨床試驗研究(RCT)以系統性評論後(systematic review: SR)的結果
	b	具有嚴格的信賴區間的個別RCT研究
	c	無論使用何種研究方法,[illegible]結果為完全正面,完全負面或完全無效的研究報告
2	a	將同質性的[illegible]以系統性評論後的結果
	b	個別世代研究或[illegible](例如低於80%follow-up)
	c	以多數結果為[illegible]研究
3	a	將同質性的個[illegible]se control studies),以系統性評論後的結果
	b	個別的個案對照研究(individual case control study)
4		病例統計報告,以及質量不足的個案對照研究
5		未經嚴謹評估的專家意見或基礎生理學,一般實驗室研究

Level 1a

英國的Oxford Centre證據應用等級

Are the valid results of this randomised trial important?



Hazard ration (存活分析; HR)
HR=1.12
95%CI=0.94-1.33
P=0.21
(沒有統計意義)

平均追蹤6.1年
服用銀杏錠的有277人出現癡呆現象
服用安慰劑的有246人出現癡呆現象

在所有病人中(n=3069)
安慰組:治療組的發生率
=2.94:3.27
P=0.21
沒有統計意義

認知功能正常
(n=2587)
安慰組:治療組的發生率=2.16:2.25
P=0.67
沒有統計意義

輕微認知障礙
(n=482)
安慰組:治療組的發生率=8.68:9.82
P=0.39
沒有統計意義

Table 2. Incidence Rates (per 100 Person-Years) and Hazard Ratios From Cox Regression Analyses: All Dementia and Subtypes of Dementia Comparing *G biloba* With Placebo for All Participants and Those Classified at Baseline With Normal Cognition and Mild Cognitive Impairment

	All Participants (N = 3069)				Baseline Normal Cognition (n = 2587)				Baseline MCI (n = 482)			
	Rate (No. of Events)				Rate (No. of Events)				Rate (No. of Events)			
Outcome	Placebo (n = 1524)	*G biloba* (n = 1545)	HR (95% CI)	*P* Value	Placebo (n = 1298)	*G biloba* (n = 1289)	HR (95% CI)	*P* Value	Placebo (n = 226)	*G biloba* (n = 256)	HR (95% CI)	*P* Value
All dementia	2.94 (246)	3.27 (277)	1.12 (0.94-1.33)	.21	2.16 (159)	2.25 (165)	1.05 (0.84-1.30)	.67	8.68 (87)	9.82 (112)	1.13 (0.85-1.50)	.39
Alzheimer without vascular dementia[a]	1.92 (161)	2.27 (192)	1.18 (0.97-1.46)	.11	1.36 (100)	1.53 (112)	1.13 (0.86-1.48)	.36	6.09 (61)	7.02 (80)	1.15 (0.83-1.61)	.40
Alzheimer with vascular dementia[b]	0.71 (59)	0.77 (65)	1.09 (0.77-1.55)	.63	5.02 (37)	5.60 (41)	1.12 (0.72-1.74)	.63	2.20 (22)	2.10 (24)	0.96 (0.54-1.71)	.89
Total Alzheimer dementia	2.63 (220)	3.04 (257)	1.16 (0.97-1.39)	.11	1.86 (137)	2.09 (153)	1.13 (0.90-1.42)	.30	8.28 (83)	9.12 (104)	1.10 (0.83-1.47)	.51
Vascular dementia without Alzheimer dementia	0.20 (17)	0.08 (7)	0.41 (0.17-0.98)	.05	0.19 (14)	0.07 (5)	0.36 (0.13-1.00)	.05	0.30 (3)	0.18 (2)	0.59 (0.10-3.51)	.56

Abb… HR, hazard ratio; MCI, mild cognitive impairment.
[a]M… unication Disorders and Stroke) criteria for probable or possible Alzheimer disease without vascular dementia.
[b]M… reatment Centers) for probable or possible vascular dementia.

在所有癡呆病人中，95%
為阿茲海默氏症

副作用發生的比率
死亡/出血/冠狀動脈疾病/中風
都沒有統計意義(p>0.05)

Table 3. Specific Serious Adverse Events

Type	No. (%)		HR (95% CI)	*P* Value
	Placebo	*Ginkgo Biloba*		
Death	188 (12.3)	197 (12.8)	1.04 (0.85-1.26)	.72
Bleeding, total	140 (9.2)	138 (8.9)	0.97 (0.77-1.23)	.81
Gastrointestinal	77 (5.1)	83 (5.4)	1.06 (0.78-1.45)	.70
All other	71 (4.7)	64 (4.1)	0.89 (0.64-1.25)	.52
CHD total	204 (13.4)	211 (13.7)	1.02 (0.84-1.24)	.83
Myocardial infarction	76 (5.0)	90 (5.8)	1.18 (0.87-1.59)	.30
Angina	99 (6.5)	107 (6.9)	1.06 (0.81-1.40)	.65
Angioplasty	65 (4.3)	79 (5.1)	1.20 (0.87-1.67)	.27
CABG	49 (3.2)	51 (3.3)	1.02 (0.69-1.52)	.90
CHD death	47 (3.1)	48 (3.1)	1.01 (0.67-1.50)	.98
Stroke, total	71 (4.7)	80 (5.2)	1.12 (0.81-1.54)	.50
Ischemic	62 (4.1)	62 (4.0)	0.99 (0.70-1.41)	.96
Hemorrhagic	8 (0.5)	16 (1.0)	1.97 (0.84-4.61)	.12
Unknown	2 (0.1)	3 (0.2)		

Abbreviations: CABG, coronary artery bypass graft; CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio.

Are the valid results of this randomized trial important?

- 預防老年人癡呆的療效
  - 安慰組 vs 銀杏組 = 249/1524 (2.94%) :277/1545 (3.27%)

失智症發生率		Relative risk reduction (RRR)	Absolute risk reduction (ARR)	Number needed to treat (NNT)
CER	EER	CER-EER / CER	CER-EER	1/ARR
2.94%	3.27%	2.94-3.27/2.94 =11.22%	0.33%	1/0.33% =304 patients
		95% CI		

NNT= 304
(每304位正常或者輕度認知障礙的病人給予240mg銀杏萃取物，在平均6.1年的追蹤下，比起安慰組可以預防一位得到癡呆症。)

Are the valid results of this randomized trial important?

- 任何原因出血的發生(adverse effect)
  - 安慰組 vs 銀杏組 = 140/1524 (9.2%) : 138/1545 (8.9%)

任何原因的出血副作用		Relative risk increase (RRI)	Absolute risk increase (ARI)	Number needed to harm (NNH)
CER	EER	CER-EER / CER	CER-EER	1/ARR
9.2%	8.9%	9.2-8.9/9.2 =0.032%	0.3%	1/0.3% =334
		95% CI □		patients

NNH=334
(每334位正常或者輕度認知障礙的病人給予240mg銀杏萃取物，在平均6.1年的追蹤下，比起為照組會有一位發生出血的機會。)

Ginkgo biloba for Preventing Cognitive Decline in Older Adults

A Randomized Trial

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Context The herbal product *Ginkgo biloba* is taken frequently with the intention of improving cognitive health in aging. However, evidence from adequately powered clinical trials is lacking regarding its effect on long-term cognitive functioning.

Objective To determine whether *G biloba* slows the rates of global or domain-specific cognitive decline in older adults.

Conclusion Compared with placebo, the use of *G biloba*, 120 mg twice daily, did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment.

GINKGO BILOBA IS MARKETED widely and used with the hope of improving, preventing, or delaying cognitive impairment associated with aging and neurodegenerative disorders such as Alzheimer disease. The primary outcome analysis from the Ginkgo Evaluation of Memory (GEM) study, the largest completed randomized, double-blind, placebo-controlled dementia prevention trial to date,[1] found that *G biloba*, 120 mg twice daily, was not effective in reducing the incidence of Alzheimer dementia or dementia overall.

Mental State Examination (3MSE), in the cognitive subscale of the Alzheimer Disease Assessment Scale (ADAS-Cog), and in neuropsychological domains of memory, attention, visual-spatial construction, language, and executive functions, based on sums of z scores of individual tests.

Results Annual rates of decline in z scores did not differ between *G biloba* and placebo groups in any domains, including memory (0.043; 95% confidence interval [CI], 0.034-0.051 vs 0.041; 95% CI, 0.032-0.050), attention (0.043; 95% CI, 0.037-0.050 vs 0.048; 95% CI, 0.041-0.054), visuospatial abilities (0.107; 95% CI, 0.097-0.117 vs 0.118; 95% CI, 0.108-0.128), language (0.045; 95% CI, 0.037-0.054 vs 0.041; 95% CI, 0.033-0.048), and executive functions (0.092; 95% CI, 0.086-0.099 vs 0.089; 95% CI, 0.082-0.096). For the 3MSE and ADAS-Cog, rates of change varied by baseline cognitive status (mild cognitive impairment), but there were no differences in rates of change between treatment groups (for 3MSE, $P=.71$; for ADAS-Cog, $P=.97$). There was no significant effect modification of treatment on rate of decline by age, sex, race, education, *APOE*E4* allele, or baseline mild cognitive impairment ($P>.05$).

Conclusion Compared with placebo, the use of *G biloba*, 120 mg twice daily, did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment.

Trial Registration clinicaltrials.gov Identifier: NCT00010803

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Can you apply this valid, important evidence about therapy in caring for your patient?

What are your patient's potential benefits and harms from the therapy?
我們病人在該治療下之可能利與弊?

Patient's expected event rate (PEER病人預期事件發生率)
直接參考文獻中相似的病人群CER 值=2. 94%

PEER= 2.94 %

Our patient has a risk of dementia of 2.94 % over a period of time equal to the duration of the trial.

【臺灣失智症的盛行率，在65歲以上老人約2~4%】

Can you apply this valid, important evidence about therapy in caring for your patient?

Do these results apply to your patient? 結果能應用在我們的病人嗎?	
Is our patients so different from those in the study that its results cannot apply? 我們研究的病人是否與文獻中病人群有本質上差異而影響結果套用?	我們病人族群是輕微認知障礙的老年人，與文獻研究中的病人族群是相似的。
Is the treatment feasible in our setting? 在我們病人是否能使用該治療?	1.衛生署適應症： 末梢血行障礙之輔助治療 2.目前國內為處方用藥。 3.目前本院circulon已停用。 【目前醫院無自費使用該藥】

臨床應用

- 1.結合實證醫學的結果、臨床專業經驗給予病人建議
- 2.結合病人價值，幫助病人做出最後的決定臨床處置

醫療現況	替代選擇
1.目前國內銀杏葉萃取物係屬於處方藥品，而列為健康食品者為銀杏果製劑。 2.目前本院沒有此藥物提供。	原發型阿茲海默症治療藥物:膽鹼酯酶抑制劑（Aricept、Exelon ）
成本效益	**病人價值觀**
1.Cerenin 40mg健保價約10元 2.粗估每年費用約12000元	1.疾病會帶來病人自卑感及憂鬱症狀 2.儘可能瞭解病人個人的感覺、需要、情感及個別價值觀，照護目標，在於維持病人的尊嚴，及病人的日常生活能力，使其免於進一步的退化

評估成果

步驟1:在提出臨床問題方面
我提出的問題是否具有臨床重要性？是，可以作為治療參考。 是否知道自己設定的問題類型?是，治療性的問題。
步驟2:在搜尋最佳證據方面
我是否從大量的資料庫來搜尋答案？是。 我是否在搜尋上愈來愈熟練了？需要加強。
步驟3:在文獻評讀方面
我可以更正確更有效率的使用一些審慎評估如:NNT?是。
步驟4:在整合證據與病患的價值觀方面
我盡力將審慎評估的結果融入治療中嗎?是。 我是否因此搜尋結果而改變了原來的治療策略？可能改變醫師開立的動機及病人購買的動機。

結論

- 研究結果
  - 目前研究證據對於使用銀杏在預防老人癡呆症上並沒有顯著的治療效果。
- 臨床證據
  - 證據強度: Level 1a
- 臨床建議
  - 目前預防老人癡呆症沒有特效藥。
  - 保持心境開朗、頭腦靈活、多運動、保持良好的社交生活，參與一些挑戰自己智慧的活動，多接觸體驗新的事物都是一些可能會帶來好處的方法。

謝謝您的聆聽!