

EBM Journal Club:
Does Ginkgo Biloba improve
memory in elder group

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報告：中醫內兒科 R2 葉兼碩

Memory loss in elder >> Dementia

- Defination
- Diagnosis
- Prognosis

Why so serious?

- 記憶力對老人的重要性？

Any way to improve memory in elder?

- 運動？
- 麻將？打電動？
- 飲食？藥物？
- ...
- 大部分人的習慣—吃什麼會好??

Any way to improve memory in elder?

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- 麻將？打電動？
- 飲食？藥物？
- ...
- 大部分人的習慣—吃什麼會好??
- 銀杏能否改善老年人的記憶力？

Background

- The standardized **Ginkgo biloba extract EGb 761®** is one of the most widely used herbal remedies for dementia and cognitive impairment and remains one of the best evaluated and characterized extracts.

DeFeudis FV, Drieu K: Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and clinical applications. Curr Drug Targets 2000, 1:25-58.

- Since 2000, according to the current ATC-classification, **Ginkgo biloba special extract is listed in the group of anti-dementia drugs** together with cholinesterase inhibitors and memantine.

EBM 5 STEPs

問	Asking [PICO format] Answerable clinical question	銀杏能否改善老年人記憶力
查	Assessing Searching the best evidence	Pub Med, Med line, Science-direct, Cochrane...
讀	Appraisal Critical Appraisal the evidence	V: validity – power, bias... I: Impact – size of effect P: Practice – usefulness in clinical
用	Apply Integrating with clinical practice	
審	Auditing Evaluate effective and efficiency	

Asking-PICO

PICO identification

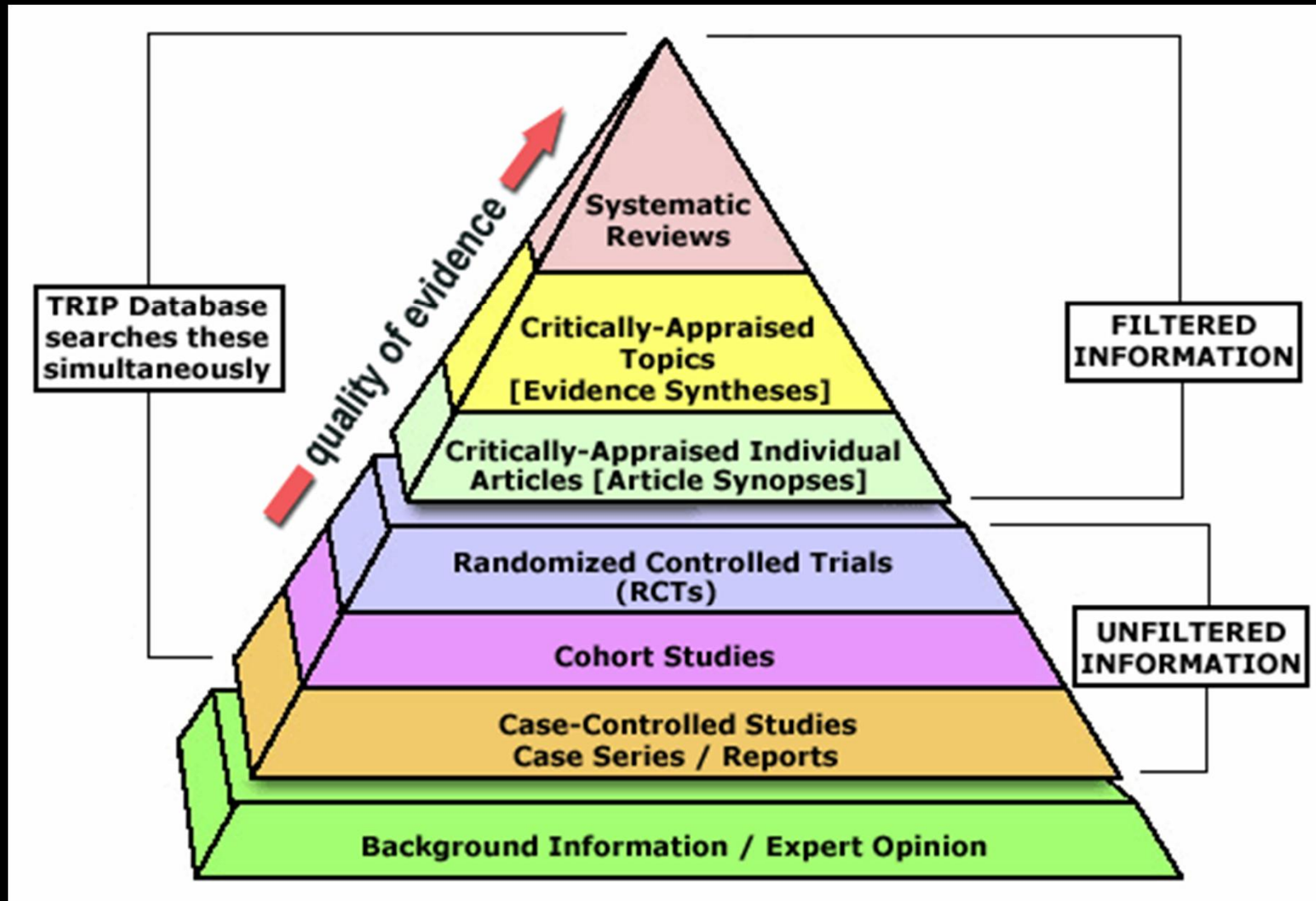
P	Problem Patient	Memory loss [dementia] in Elders (> 65 y/o)
I	Intervention	Ginkgo Biloba PO
C	Comparison	Ginkgo Biloba V.S. Placebo
O	Outcome	Improve memory or not

Searching Key word

- Ginkgo Biloba,
- Memory, Dementia
- Elder, old age

Assessing

- EBM 金字塔



PubMed

- Ginkgo biloba and dementia
 - Systemic review: 16 article [2001-2011]

Cochrane Database Syst Rev. 2009 Jan 21;(1):CD003120.

Ginkgo biloba for cognitive impairment and dementia.

Birks J, Grimley Evans J.

PubMed

- Ginkgo biloba and dementia
 - Systemic Review: 42 article [1998-2011]

BMC Geriatr. 2010 Mar 17;10:14.

Effects of Ginkgo biloba in dementia: systematic review and meta-analysis.

Weinmann S, Roll S, Schwarzbach C, Vauth C, Willich SN.

Fortschr Neurol Psychiatr. 2009 Sep;77(9):494-506. Epub 2009 Jul 20.

Ginkgo biloba extract EGb 761 in the treatment of dementia: evidence of efficacy and tolerability. [Article in German]

Kasper S, Schubert H.

Appraisal

- CEBM[2005, Oxford]
- Jadad scale
- NHS-CASP

Systemic Review Appraisal sheet

- 1) What question [PICO] did the systemic review address?
- 2) Is it unlikely that important, relevant studies were missed
- 3) What the criteria used to select articles for inclusion appropriate?
- 4) Were the included studies sufficiently valid for the type of question asked?
- 5) Were the results similar from study to study?
- 6) How are the result presented?

Effects of Ginkgo biloba in dementia: systematic review and meta-analysis

Stefan Weinmann, Stephanie Roll, Christoph Schwarzbach,
Christoph Vauth, Stefan N Willich

BMC Geriatrics 2010, 10:14

Impact Factor:

Background

- Most previous reviews have shown inconsistent results and fail to draw firm conclusions whether Ginkgo biloba has patient-relevant benefits in people with a diagnosis of dementia.

Ernst E, Pittler MH: Ginkgo biloba for vascular dementia and Alzheimer's disease: updated systematic review of double-blind, placebo-controlled, randomized trials. *Perfusion* 2005, 18:388-392.

- A major limitation of the available Cochrane Review on the effectiveness of Ginkgo biloba is the combined evaluation of cognitive decline and dementia. No subgroup analyses were performed.

Birks J: Ginkgo biloba for cognitive impairment and dementia. *Cochrane Database Syst Rev* 2009, 21(1):CD003120.

Background

- German Health Technology Assessment Institute IQWiG (Institute for Quality and Efficiency in Health Care) published a favorable report on the effectiveness of Ginkgo biloba, which was, however, limited to Alzheimer's disease and contradicted the Cochrane review.

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen:
Ginkgohaltige Präparate bei Alzheimer Demenz. Abschlussbericht A05-
19B. Köln 2008.

- We performed a systematic review on the effects of Ginkgo biloba in Alzheimer's disease as well as vascular and mixed dementia covering a variety of outcome domains.

Methods

- Data sources
 - Database: Medline, EMBASE, PsycINFO, CINAHL, the Cochrane Database of systemic Reviews, Cochrane Controlled Trials Register.

Methods

- Terms
 - Dementia
 - Dementia; Alzheimer
 - Ginkgo biloba
 - ginkgo; ginko; gingko; bilo- balid; tebonin; egb 761; li 1370
 - Identify clinical trial
 - (clinical AND trial*); random*; placebo*; (controlled AND trial*); (mul- timent* AND stud*); (comparative AND stud*); follow- up; (research AND design)

Method

- Selection
 - Controlled clinical trials, with or without randomization
 - Assessing the effects of treating people with a diagnosis of Alzheimer's disease, vascular or mixed dementia according to internationally valid diagnostic criteria
 - With a standardized Ginkgo biloba extract.

Method

- Inclusion Criteria
 - internationally accepted diagnostic for the dementia diagnosis
 - minimum treatment duration of 12 weeks
 - minimum number of participants of ten per group
 - availability of a full-text publication

Method

- Exclusion Criteria
 - studies with a majority of people with specific types of non-vascular and non-Alzheimer's dementia
 - publication language other than English, German, French, Italian or Spanish

Data extraction and critical appraisal

- Study selection and appraisal of studies were performed independently by two researchers
- Information was extracted via a standardized checklist

Result

- Search in MEDLINE, EMBASE, Cochrane, PsycINFO and CINAHL yielded 754 clinical publications.
- 63 publications were included in the full-text screening
- 17 publications reporting 9 individual studies, all using the standardized extract EGb 761 .

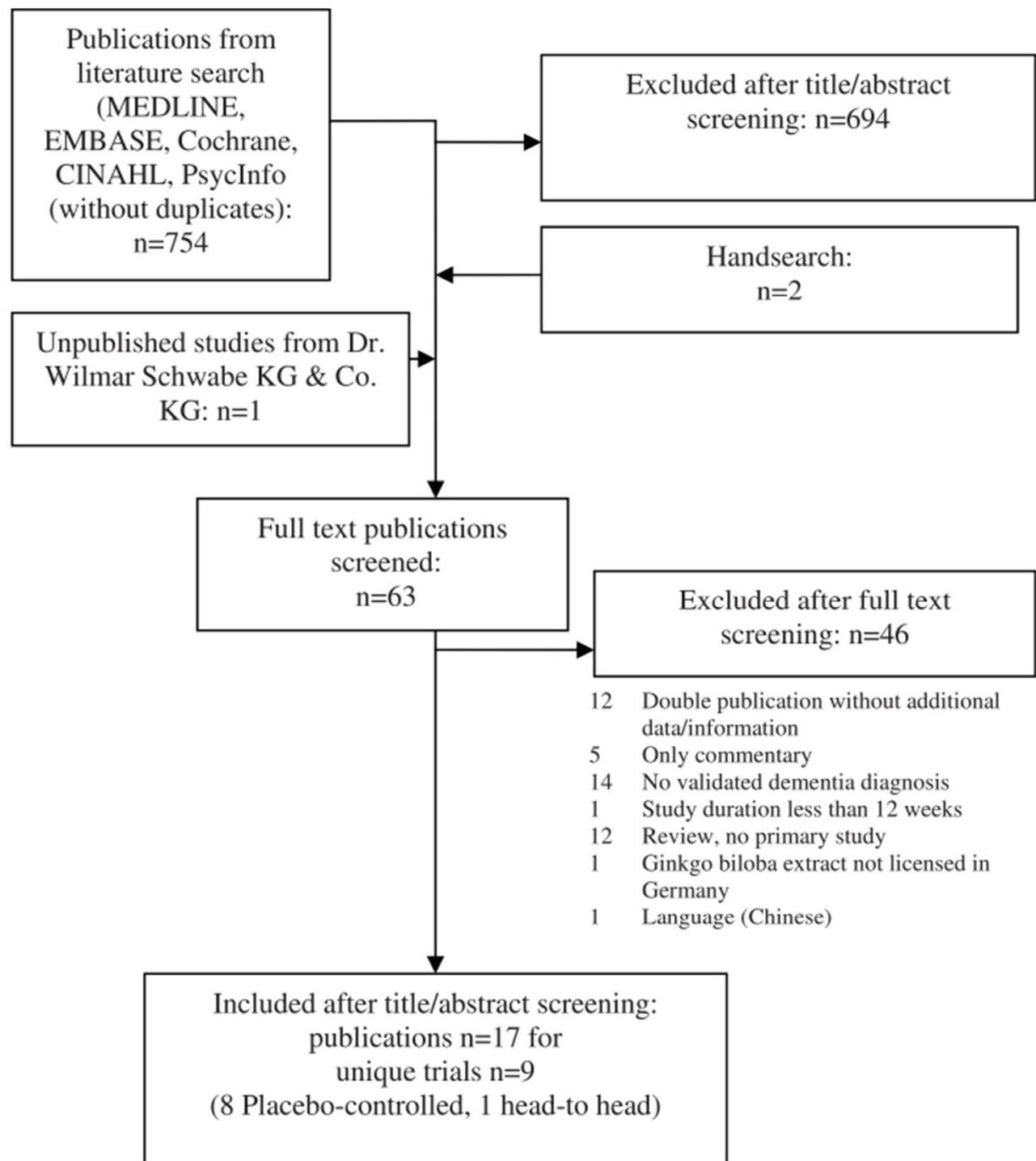


Figure 1 Flow chart of study identification and selection.

Study characteristic

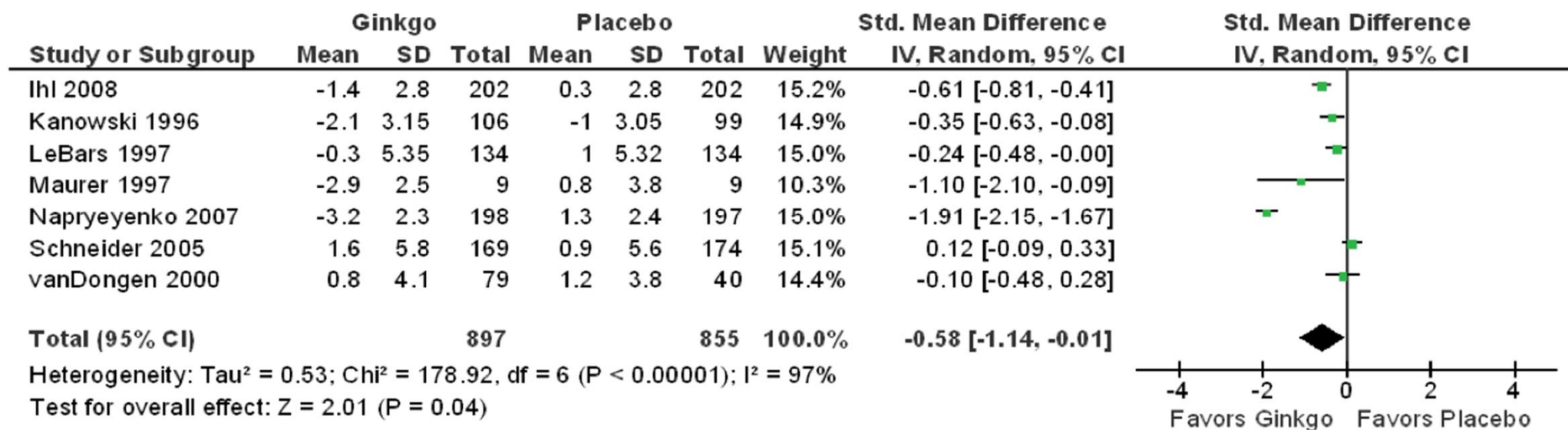
- All included studies were randomized
- All studies were described as double-blind
- 8 studies were placebo-controlled
- 1 study was a head-to-head trial with donepezil as comparison group

Table 1 Methodological quality of included studies

Study Authors, date	Randomization/ allocation concealment	Blinding of patients/outcomes assessment	Prior estimate of sample size	Withdrawals per group reported	ITT analysis adequate	Report of measures of precision	Data inconsistencies	Funding reported
Kanowski et al. 1996/2003 [29,36]	Yes/yes	Yes/yes	Partly ^a	Partly ^b	Yes	Yes	No	No
Le Bars et al. 1997/2000 [30,37]	Yes/yes	Yes/unclear	Yes	Yes	Yes	Yes	No	Yes
Maurer et al. 1997 [31]	Yes/unclear	Yes/unclear	No	Yes	No	No	No	No
van Dongen et al. 2000 [34,45]	Yes/yes	Yes/yes	Yes	Yes	No	Yes	Yes ^c	Yes
Schneider et al. 2005 [33]	Yes/yes	Yes/yes	Yes	Yes	Yes	Yes	No	Yes
Yancheva et al 2009 [35]	Yes/unclear	Yes/unclear	No	Yes	Yes	Yes	Yes	Yes
Napryeyenko et al. 2007 [32]	Yes/unclear	Yes/unclear	Yes	Yes	Yes	Yes	No	Yes
McCarney et al. 2008 [2]	Yes/yes	Yes/yes	Partly ^a	Yes	Yes	Yes	No	Yes
Ihl et al. 2009	Yes/yes	Yes/yes	No	Yes	Yes	Yes	No	Yes

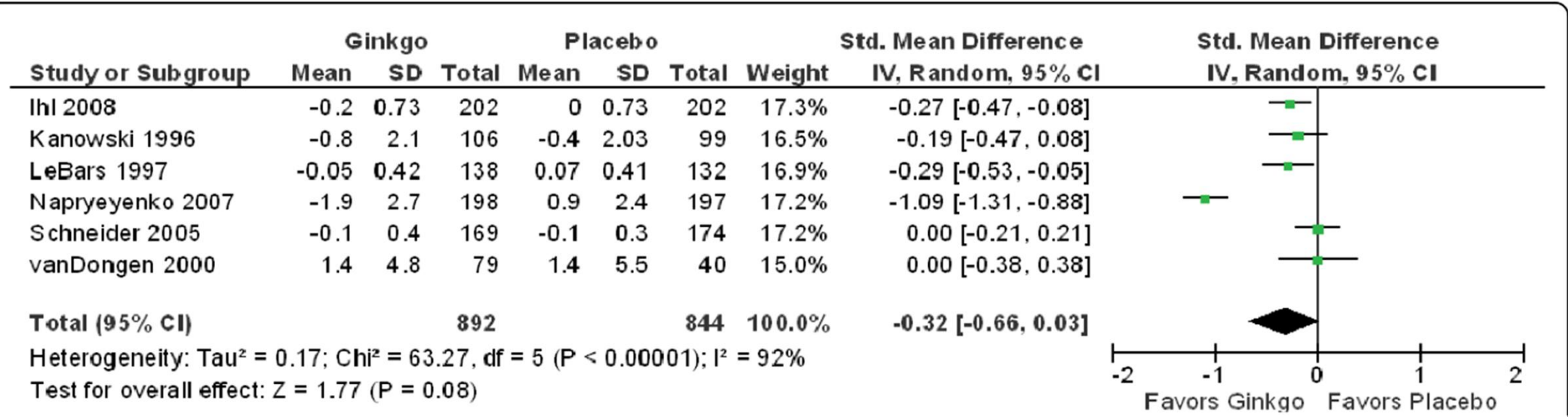
a: Less patients were included than planned; b: Drop-out rates were reported, but without reference to study arm; c: Multiple re-randomization schemes. ITT = Intent-to-treat analysis.

- Trials were of 12 to 52 weeks duration and included 2372 patients in total
- Heterogeneity among studies was high.



ADAS-cog=Alzheimer's disease Assessment Scale cognitive subscale; ITT=intent-to-treat; LOCF=last observation carried forward; SD=standard deviation; SKT=Syndrom Kurz-Test; 95% CI=95% confidence interval.

Figure 2 ITT/LOCF change scores for cognition outcomes (ADAS-cog, SKT) by individual trial and pooled standardized mean difference compared with placebo.



ITT=intent-to-treat; LOCF=last observation carried forward; SD=standard deviation; 95% CI=95% confidence interval.

Figure 3 ITT/LOCF change scores for activities of daily living outcomes by individual trial and pooled standardized mean difference compared with placebo.

Discussion

- Withdraws
 - No different btw medication and placebo

Discussion

- We found a statistically significant advantage of Ginkgo biloba compared to placebo in improving cognition for the whole group of patients with Alzheimer's disease, vascular or mixed dementia.

Discussion

- Regarding activities of daily living, there was no significant difference for the whole dementia group.
- However, in the subgroup of patients with Alzheimer's disease, the advantage of Ginkgo biloba compared to placebo was statistically significant.

Discussion

- There was no consistent evidence of a benefit of Ginkgo biloba in the treatment of neuropsychiatric symptoms.
- However, the presence of psychological or behavioral symptoms in dementia may be an effect modifier.

Author's conclusion

- Statistically significant advantage of Ginkgo biloba compared to placebo in improving cognition for the whole group of patients with Alzheimer's disease.

Apply

Auditing

- 我提出的問題是否具有臨床重要性?
 - 我是否明確的陳述了我的問題?
- 我是否已盡全力力搜尋?
 - 我是否從大量的資料庫來搜尋答案?
- 我是否盡全力做評讀?
 - 評讀後,我是否做出了結論?
- 我是否覺得這個進行實證醫學的過程是值得的?
- 我還有那些問題或建議?