Appendix 15: Included/excluded study information tables

Table 1: Included/excluded studies table for review of lifestyle or other interventions that can prevent or delay onset of dementia

Table 2: Included studies table for review of diagnostic test accuracy

Table 3: Included/excluded studies table for review of strategies for promoting independence

Table 4: Included/excluded studies table for review of psychosocial interventions for the treatment of cognitive symptoms of dementia

Table 5: Included/excluded studies table for the review of acetylcholinesterase inhibiting drugs or memantine for the treatment of cognitive symptoms of non-Alzheimer's dementia or MCI

Table 6: Included/excluded studies table for the review of medicine other than acetylcholinesterase inhibiting drugs or memantine for the treatment of cognitive symptoms of dementia

Table 7: Included/excluded studies table for the review of psychosocial interventions for the management of behaviour that challenges

Table 8: Included/excluded studies table for the review of psychological interventions for co-morbid emotional disorders

Table 9: Included/excluded studies table for the review of pharmacological interventions for non-cognitive symptoms of dementia

Table 10: Included/excluded studies table for review of interventions for carers of people with dementia
Table 1: Included/excluded studies table for review of lifestyle or other interventions that can prevent or delay onset of dementia

### Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Antihypertensives vs Placebo</th>
<th>Aspirin vs placebo</th>
<th>DHEA vs placebo</th>
<th>Estradiol vs Placebo</th>
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<tbody>
<tr>
<td>HOPE2002</td>
<td>CLARKE2003</td>
<td>BARNHART1999</td>
<td>BAGGER2005</td>
</tr>
<tr>
<td>PROGRESS2003</td>
<td></td>
<td>HUPPERT2000</td>
<td>VISCOLI2002</td>
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<tr>
<td>SCOPE2003</td>
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<td>SHEP1991</td>
<td></td>
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<tr>
<td>SYST-EUR1999</td>
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<td>UK-MRC1996</td>
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</tr>
<tr>
<td>Folic acid vs placebo</td>
<td></td>
<td></td>
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<tr>
<td>BRYAN2002</td>
<td>MILLER2005</td>
<td>HENDERSON2005</td>
<td>DECRAEN2005</td>
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<tr>
<td>FIORAVANTI1997</td>
<td></td>
<td>LOW2005</td>
<td>ETMINAN2003</td>
</tr>
<tr>
<td>MALOUF2003</td>
<td></td>
<td>YAFFE2005</td>
<td>INTVELD2001</td>
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<tr>
<td>Oestrogen + progestin vs Placebo</td>
<td>PAN2003</td>
<td>WISNIEWSKI2002</td>
<td>CLARKE2003</td>
</tr>
<tr>
<td>GRADY2002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHUMAKER2003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B12 vs No treatment</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>KWOK1998</td>
<td>BRYAN2002</td>
<td>BRYAN2002</td>
<td></td>
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<td></td>
<td>GARCIA2004</td>
<td>MALOUF2003A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HVAS2004</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Characteristics of Included Studies

#### BAGGER2005

**Methods**
- Study Type: Cohort study
- Study Description: Retrospective cohort study
- Interviewer who performed cognitive tests were blinded to HRT status
- Type of Analysis: Completers only
- Blindness: Single blind
- Duration (days):
- Followup: 5, 11 or 15 years after completion of previous trial
- Setting: Women who previously participated in one of four previous HRT trials between 1983-1996 in Denmark
- Notes: Detailed methods described elsewhere

<table>
<thead>
<tr>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
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<tbody>
<tr>
<td>n = 343</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Age: Mean 65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex: all females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusions: At entry to previous studies: absence of menopause any time in past 6 mths, history of sex hormone treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Details described elsewhere</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Data Used**
- Blessed Orientation Memory-Concentration Test

**Group 1 N = 107**
- Placebo with - Had received placebo during trials and did not take HRT after completion

**Group 2 N = 154**
- Oestrogen with - Short-term HRT users: received HRT during trials for 2-3 years, discontinued after completion

**Group 3 N = 78**
- Oestrogen with - Long-term/current users: Initiated or continued HRT for >=3 yrs after completion of original trials, or current HRT for >=1 yr

#### BARNHART1999

**Methods**
- Study Type: Cohort study
- Study Description: Retrospective cohort study
- Interviewer who performed cognitive tests were blinded to HRT status
- Type of Analysis: Completers only
- Blindness: Single blind
- Duration (days):
- Followup: 5, 11 or 15 years after completion of previous trial
- Setting: Women who previously participated in one of four previous HRT trials between 1983-1996 in Denmark
- Notes: Detailed methods described elsewhere

<table>
<thead>
<tr>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
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</thead>
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<tr>
<td>n = 107</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Age: Mean 65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex: all females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusions: At entry to previous studies: absence of menopause any time in past 6 mths, history of sex hormone treatment</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Details described elsewhere</td>
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<td></td>
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</tr>
</tbody>
</table>

**Data Used**
- Blessed Orientation Memory-Concentration Test

**Group 1 N = 107**
- Placebo with - Had received placebo during trials and did not take HRT after completion

**Group 2 N = 154**
- Oestrogen with - Short-term HRT users: received HRT during trials for 2-3 years, discontinued after completion

**Group 3 N = 78**
- Oestrogen with - Long-term/current users: Initiated or continued HRT for >=3 yrs after completion of original trials, or current HRT for >=1 yr

**Notes**
<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n=60</th>
<th>Data Used</th>
<th>Group 1 N=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: Double blind</td>
<td></td>
<td>Digit Symbol Substitution Test</td>
<td>DHEA with . Mean dose 50mg - Daily capsule of DHEA at 20.00 each evening</td>
</tr>
<tr>
<td>Duration (days): Mean 90</td>
<td></td>
<td>Symbol Coping Test</td>
<td>Group 2 N=30</td>
</tr>
<tr>
<td>Setting: perimenopausal women, USA</td>
<td></td>
<td></td>
<td>Placebo with - Identical capsule as the study medication</td>
</tr>
<tr>
<td>Info on Screening Process: 6 people dropped out because of adverse effects</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Diagnosis:**

1. Age: Mean 67
2. Sex: 66 females

**Exclusions:**

- <2>12 months of amenorrhea after previous history of normal regular menstrual cycle, presence of a score of moderate to severe for less than 2 target symptoms (i.e. fatigue, lack of energy, anxiety, tension, irritability, depression, insomnia, forgetfulness, concentration difficulties, decreased libido, global reports of decreased sense of well being), contraindication to hormonal replacement therapy, exposure to injectable or implantable sex steroid within 6 months, used antidepressants and/or anxiolytics, current diagnosis of major psychiatric disorder, diabetes mellitus, hypercholesterolemia, cardiovascular disease, abnormal renal or liver function

---

<table>
<thead>
<tr>
<th>Results from this paper:</th>
<th>n=60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Validity:</td>
<td></td>
</tr>
<tr>
<td>1.1 adequately addressed</td>
<td></td>
</tr>
<tr>
<td>1.2 poorly addressed</td>
<td></td>
</tr>
<tr>
<td>1.3 not reported</td>
<td></td>
</tr>
<tr>
<td>1.4 adequately addressed</td>
<td></td>
</tr>
<tr>
<td>1.5 adequately addressed</td>
<td></td>
</tr>
<tr>
<td>1.6 well covered</td>
<td></td>
</tr>
<tr>
<td>1.7 adequately addressed</td>
<td></td>
</tr>
<tr>
<td>1.8 10% dropped out</td>
<td></td>
</tr>
<tr>
<td>1.9 not addressed</td>
<td></td>
</tr>
<tr>
<td>1.10 not applicable</td>
<td></td>
</tr>
<tr>
<td>Overall Assessment of the Study:</td>
<td></td>
</tr>
<tr>
<td>2.1 1+</td>
<td></td>
</tr>
<tr>
<td>2.2 favours treatment</td>
<td></td>
</tr>
<tr>
<td>2.3 no</td>
<td></td>
</tr>
<tr>
<td>2.4 don't know</td>
<td></td>
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</table>

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<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n=211</th>
<th>Data Used</th>
<th>Group 1 N=74</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: 3 age groups: younger (20-30 years), middle (45-55 years), older (65-92 years)</td>
<td></td>
<td>MMSE ADAS-Cog</td>
<td>Vitamin B12 + Folate with - 2mg of folic acid and 1mg vitamin B12</td>
</tr>
<tr>
<td>Blindness: Double blind</td>
<td></td>
<td></td>
<td>Group 2 N=75</td>
</tr>
<tr>
<td>Duration (days): Mean 150</td>
<td></td>
<td></td>
<td>Placebo with</td>
</tr>
<tr>
<td>Setting: Australia, Commonwealth Scientific and Industrial Research Organisation - healthy women selected from the Australian electoral roll</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Age: Range 20-92</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Sex: all females</td>
<td></td>
<td></td>
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</table>

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<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n=149</th>
<th>Data Used</th>
<th>Group 1 N=74</th>
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</thead>
<tbody>
<tr>
<td>Study Description: medication in blister packs identical for each participant to conceal allocation. Telephone randomisation system.</td>
<td></td>
<td>MMSE ADAS-Cog</td>
<td>Vitamin B12 + Folate with - 2mg of folic acid and 1mg vitamin B12</td>
</tr>
<tr>
<td>Blindness: Double blind</td>
<td></td>
<td></td>
<td>Group 2 N=75</td>
</tr>
<tr>
<td>Duration (days): Mean 150</td>
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<td></td>
<td>Placebo with</td>
</tr>
<tr>
<td>Setting: Australia, Commonwealth Scientific and Industrial Research Organisation - healthy women selected from the Australian electoral roll</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td>56% Alzheimer’s disease</td>
</tr>
</tbody>
</table>
### Results from this paper:

**Internal Validity:**
- 1.1 Adequately addressed
- 1.2 Adequately addressed
- 1.3 Well covered
- 1.4 Well covered
- 1.5 Adequately addressed
- 1.6 Well covered
- 1.7 Well covered
- 1.8 4.6% dropped out
- 1.9 Not addressed
- 1.10 Not addressed

**Overall Assessment of the Study:**
- 2.1 1+
- 2.2 either treatment or placebo
- 2.3 yes
- 2.4 to some extent

**Conclusions:** Neither of the cognitive tests or ADL were found to be significantly altered by treatment

---

### DECRAEN2005

**Study Type:** Systematic Review

<table>
<thead>
<tr>
<th>Blindness: Double blind</th>
<th>Duration (days): Mean 84</th>
</tr>
</thead>
</table>

**Setting:** Community dwelling people in UK

**Info on Screening Process:** 174 screened - 4 excluded, 170 entered run in - 21 dropped out because of poor compliance, 7 dropped out after randomization

**Exclusions:** no cognitive impairment or dementia, diagnosis of fronto-temporal dementia, Parkinson's disease, Huntingdon's disease, normal pressure hydrocephalus, taking study treatments and/or have contraindications to them, individuals with aspirin sensitivity or peptic ulcer, life threatening disease or cancer, concern over their likely compliance, resident in a nursing home

**Baseline:** MMSE = 21 ADAS-Cog = 28

---

### ETMINAN2003

**Study Type:** Systematic Review

**Blindness:**

**Duration (days):**

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Well covered
- 1.3 Poorly addressed
- 1.4 Not addressed
- 1.5 Adequately addressed

**Overall assessment of the study:**
- 2.1 -
- 2.2 Favours NSAIDs
<table>
<thead>
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<th>Study Type: Systematic Review</th>
<th>Duration (days):</th>
<th>Blindness:</th>
<th>Results from this paper:</th>
<th>Internal Validity:</th>
<th>Overall assessment of the study:</th>
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<tbody>
<tr>
<td>ETMINAN2003</td>
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<th>Blindness:</th>
<th>Setting:</th>
<th>Results from this paper:</th>
<th>Internal Validity:</th>
<th>Overall Assessment of the Study:</th>
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<tbody>
<tr>
<td>FIORAVANTI1997</td>
<td>Mean 60</td>
<td>Double blind</td>
<td>participants with mild to moderate cognitive decline living at home or in a community, Italy</td>
<td></td>
<td></td>
<td>2.1++ 2.2</td>
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<table>
<thead>
<tr>
<th>Study Type: Cohort study</th>
<th>Duration (days):</th>
<th>Blindness:</th>
<th>Setting:</th>
<th>Results from this paper:</th>
<th>Internal Validity:</th>
<th>Overall Assessment of the Study:</th>
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<tr>
<td>GARCIA2004</td>
<td></td>
<td>Double blind</td>
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<table>
<thead>
<tr>
<th>Group</th>
<th>N= 16</th>
<th>Folic acid with . Mean dose 15 mg/day</th>
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<tbody>
<tr>
<td>Group 2</td>
<td>N= 14</td>
<td>Placebo with - same modality as treatment group</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 10</th>
<th>Vitamin B12 with . Mean dose 1000 micro grams - Monthly intramuscular injections of 1000 micrograms of</th>
</tr>
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<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
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<tbody>
<tr>
<td>Randi Memory Test</td>
<td>Folic acid with . Mean dose 15 mg/day</td>
<td>Placebo with - same modality as treatment group</td>
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<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia Rating Scale</td>
<td>Vitamin B12 with . Mean dose 1000 micro grams - Monthly intramuscular injections of 1000 micrograms of</td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tHcy</td>
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</table>

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia Rating Scale</td>
<td>Folic acid with . Mean dose 15 mg/day</td>
<td>Placebo with - same modality as treatment group</td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tHcy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Setting: Canada

Diagnosis:
Exclusions: abnormal Cobalamin levels, cognitive impairment, not elevated MMA levels, impaired renal function
Baseline: MMSE: Placebo = 28.2 Cobalamin = 28.2;
Dementia Rating Scale: Placebo = 139 Cobalamin = 140.4

cobalamin for 6 months

Group 2 N= 12
Placebo with . Mean dose 1000 micro grams - Monthly intramuscular injections of 1000 micro grams of saline for 6 months

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Not reported
1.3 Not reported
1.4 Well covered
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Well covered
1.8 Vitamin B12 = 20 % dropped out Placebo = 0% dropped out
1.9 Not addressed
1.10 Not applicable

Overall Assessment of the Study:
2.1 2+
2.2 favours treatment
2.3 maybe
2.4 yes

GRADY2002

Study Type: RCT (individual)
Study Description: Randomisation stratified by clinical centre
Blindness: Double blind
(intividual)
Duration (days): Mean 1533
Followup: Every four months
Setting: Ancillary study of the Heart and Estrogen/progestin Replacement Study at 10 centres, USA
Info on Screening Process: 1328 enrolled and randomised; 265 withdrawals (119 deaths, 50 unable to complete testing due to health, 68 withdrew consent, 24 failed to attend final test)

n= 1063
Age: Mean 67 Range 44-79
Sex: all females
Diagnosis:
Exclusions: Age >=80 yrs; no established cardiovascular disease; lack of intact uterus.
Details given elsewhere.
Baseline: Not given

Group 1 N= 517
Oestrogen with . Mean dose 0.625 + 2.5mg - Oral conjugated estrogen (0.625mg) + medroxyprogesterone acetate (2.5mg) in one tablet daily

Group 2 N= 546
Placebo with . Mean dose 3.125mg - Identical placebo

Data Used
Geriatric Depression Scale
Trails B
Word List Recall
Word List Memory
Boston naming
Verbal fluency
3MSE (Modified Mini-Mental Status)

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Adequately addressed
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Well covered
1.8 22% hormone group, 18% placebo drop out
1.9 Not addressed
1.10 Not addressed

Overall Assessment of the Study:
2.1 1-
2.2 Unsure
2.3 Unsure

### HENDERSON2005

**Study Type:** Case control study  
**Study Description:** Odds ratios for AD given HRT or no treatment, adjusted for age, education and race  
**Blindness:** Open  
**Duration (days):**  
**Setting:** Ancillary study to Multi-Institutional Research in Alzheimer Genetic Epidemiology (MiRAGE) study in the USA  
**Info on Screening Process:** 1351 screened; 380 excluded (oestrogen use, age, education, ethnicity and ApoE genotype unknown)  

### HOPE2002

**Study Type:** RCT (individual)  
**Study Description:** Two by two factorial design. No details on randomisation or allocation concealment.  
**Blindness:** Double blind  
**Duration (days):**  
**Followup:** 4.5 years (mean)  
**Setting:** 267 hospitals in 19 countries, coordinated by the Canadian Cardiovascular Collaboration in Hamilton, Canada.  
**Info on Screening Process:** No details  
<table>
<thead>
<tr>
<th>n</th>
<th>Group 1 N= 464</th>
<th>Group 2 N= 465</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 66</td>
<td>Antihypertensive with . Mean dose 10mg - Entered 7-10 Ramipril (2.5mg) run-in phase, 10-14 days of placebo. Then 2.5mg daily for 1 week, 5mg daily for 3 weeks, 10mg for the remainder of the study.</td>
<td>Placebo with - Matching placebo, same procedure.</td>
</tr>
<tr>
<td>Sex: no information</td>
<td>100% High risk for cardiovascular events</td>
<td></td>
</tr>
</tbody>
</table>
**Exclusions:** Taking either an angiotensin converting enzyme inhibitor or vitamin e; had heart failure or a known left ventricular ejection fraction of less than 0.40, known proteinuria, or uncontrolled hypertension; or had a previous stroke or myocardial infarction less than one month before enrolment in the study. |  

### HUPPERT2000

**Study Type:** Systematic Review  
**Blindness:**  
**Duration (days):**  
**Results from this paper:**  
**Internal Validity:**  
1.1 Well covered  
1.2 Well covered  
1.3 Well covered  
1.4 Well covered  
1.5 Well covered  
**Overall assessment of the study:** ++
**HVAS2004**

Study Type: RCT (individual)
Study Description: Intention to treat
Blindness: Double blind
Duration (days): Followup: 18 months
Setting: Denmark, participants were borderline between cognitive impairment and normal

- Group 1 N= 70
  - Vitamin B12 with . Mean dose 1 mg - Injections of 1 mg cyanocobalamin weekly for 4 weeks

- Group 2 N= 70
  - Placebo with . Mean dose 1 ml - 1 ml isotonic sodium chloride weekly for 4 weeks

Followup: 18 months
Setting: Denmark, participants were borderline between cognitive impairment and normal

Duration (days):
Blindness: Double blind
Study Type: RCT (individual)
Study Description: Intention to treat

Results from this paper:

- Internal Validity:
  - 1.1 Well covered
  - 1.2 Not reported
  - 1.3 Not addressed
  - 1.4 Well covered
  - 1.5 Adequately addressed
  - 1.6 Adequately addressed
  - 1.7 Adequately addressed
  - 1.8 treatment group =7.1% drop out, placebo group =1.4%
  - 1.9 Not addressed
  - 1.10 Not applicable

Overall Assessment of the Study:
- 2.1 1+
- 2.2 favours treatment
- 2.3 yes
- 2.4 yes

**INTVELD2001**

Study Type: Cohort study
Study Description: Prospective, population based cohort study of use of NSAID (with the exception on aspirin) for reducing risk of AD and VaD
Blindness: Duration (days):
Followup: average of 6.8 years
Setting: Rotterdam, the Netherlands - part of a study of neurologic, cardiovascular, locomotor, and ophthalmologic diseases in elderly persons
Info on Screening Process: 7528 screened and examined for dementia, 7046 free of dementia57 subjects excluded because of less than 6 months of data on their history of medication use

**KWOK1998**

Study Type: RCT (individual)
Study Description: Subjects randomized by Hong Kong Identity Card numbers which were randomly assigned. Last digit even number -

- Group 1 N= 23
  - Vitamin B12 with - Three doses of cyanocobalamin 1 mg given intramuscularly in the first week, one
control, odd number - treatment
Blindness: No mention
Duration (days):
Followup: 3-6 months
Setting: Majority were vegetarians living in their own homes or homes for aged in Hong Kong. Minority were those with subnormal cobalamin levels in hospital

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 27</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment with - Received no intervention and advised not to take any oral vitamin supplements</td>
<td></td>
</tr>
</tbody>
</table>

Dose weekly for a further 3 weeks, then one monthly dose thereafter

| Diagnosis: |
| 20% Unspecified dementia |
| Exclusions: Participants who could not cooperate with neuropsychological tests because of severe confusion or communication problems, participants with anaemia, unstable medical conditions and signs of subacute combined degeneration of cord |

Baseline: MMSE: Treatment = 22.2 Control = 23.8; Visual Memory: Treatment = 12.7 Control = 15.7; Verbal Memory: Treatment = 7.8 Control = 11.4; Digit Span: Treatment = 10.4 Control = 11.6

Results from this paper:
Internal Validity:
1.1 Adequately addressed
1.2 Adequately addressed
1.3 Adequately addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Poorly addressed
1.7 Adequately addressed
1.8 5.7%
1.9 Not addressed
1.10 Not addressed

Overall Assessment of the Study:
2.1 1+
2.2 in favour of treatment or control
2.3 no
2.4 to some extent

MALOUF2003
Study Type: Systematic Review
Blindness:
Duration (days):

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Adequately addressed
1.4 Poorly addressed
1.5 Adequately addressed

Overall assessment of the study:
2.1 +
2.2 unsure
Results from this paper:
Internal Validity:
1.1  Well covered
1.2 Well covered
1.3 Well covered
1.4 Well covered
1.5 Well covered

Overall assessment of the study:
2.1 ++
2.2

MALOUF2003A
Study Type: Systematic Review

Blindness:
Duration (days):

Results from this paper:
Internal Validity:
1.1  Well covered
1.2 Adequately addressed
1.3 Adequately addressed
1.4 Poorly addressed
1.5 Poorly addressed

Overall assessment of the study:
2.1 ++
2.2

MILLER2005
Study Type: Systematic Review

Blindness:
Duration (days):

Results from this paper:
Internal Validity:
1.1  Well covered
1.2 Adequately addressed
1.3 Adequately addressed
1.4 Poorly addressed
1.5 Poorly addressed

Overall assessment of the study:
2.1 +
2.2 Against vitamin E

MORRIS2005
### PAN2003

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>Group 1</th>
<th>N= 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: Randomisation by computer-generated table. No further blinding details given.</td>
<td>Oestrogen (estradiol) with . Mean dose 0.625mg - Conjugated equine estrogens, daily</td>
<td></td>
</tr>
<tr>
<td>Blindness: Single blind</td>
<td>Progestin with . Mean dose 5mg - Medroxyprogesterone acetate, daily</td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 180</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Setting: Single centre in Taiwan</td>
<td>Group 2</td>
<td>N= 17</td>
</tr>
<tr>
<td>Info on Screening Process: 50 enrolled, 10 withdrawals</td>
<td>Tibolone with . Mean dose 2.5mg - Tibolone, daily</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>n= 40</th>
<th>Data Used</th>
<th>MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 52</td>
<td>Incident AD</td>
<td></td>
</tr>
<tr>
<td>Sex: all females</td>
<td>Vitamin E with - sample divided into quintiles with the first quintile corresponding to the lowest intake of vitamin E: α-tocopherol: q 1 (n = 740), q 2 (n = 742), q 3 (n = 750), q 4 (n = 742), q 5 (n = 742); γ-tocopherol: q 1 (n = 744), q 2 (n = 742), q 3 (n = 746), q 4 (n = 742), q 5 (n = 74)</td>
<td></td>
</tr>
</tbody>
</table>

### Data Used

- **Incident AD**

<table>
<thead>
<tr>
<th>n= 3718</th>
<th>Group 1</th>
<th>N= 371</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 74</td>
<td>Vitamin E with - sample divided into quintiles with the first quintile corresponding to the lowest intake of vitamin E: α-tocopherol: q 1 (n = 740), q 2 (n = 742), q 3 (n = 750), q 4 (n = 742), q 5 (n = 742); γ-tocopherol: q 1 (n = 744), q 2 (n = 742), q 3 (n = 746), q 4 (n = 742), q 5 (n = 74)</td>
<td></td>
</tr>
<tr>
<td>Sex: 1410 males 2308 females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusions: &lt;65 years of age,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Setting: Chicago Health and Aging Project,

began with a door to door census in 1993

Info on Screening Process: 6158 screened, 1298 died before follow up, 213 excluded because their food questionnaire was invalid, 460 completed the food questionnaire >2.5 years after baseline. 3718 available for analysis, random sample of 1141 clinically evaluated for AD

### Results from this paper:

**INTERNAL VALIDITY:**
- 1.1 Adequately addressed
- 1.2 Adequately addressed
- 1.3 Adequately addressed
- 1.4 Adequately addressed
- 1.5 60.4%
- 1.6 Not addressed
- 1.7 Adequately addressed
- 1.8 Adequately addressed
- 1.9 Adequately addressed
- 1.10 Well covered
- 1.11 Well covered
- 1.12 Well covered
- 1.13 Adequately addressed
- 1.14 Well covered

**OVERALL ASSESSMENT OF THE STUDY:**
- 2.1 2 +
- 2.2 no
- 2.3 yes

Conclusions: Vitamin E intake from food linearly and inversely associated with 4 year risk of developing AD in a model adjusted for age, sex, race, APOE-e4, education, frequency of participation in cognitive activities and fat intake. High intake of Vitamin E was also significantly associated with a slower decline in cognitive score
### PROGRESS2003

**Study Type:** RCT (individual)

**Study Description:** Allocation to treatment done by fax from clinical center to study randomisation center in NZ. Stratified by centre, sex, age, blood pressure, diagnosis

**Type of Analysis:** Intention to Treat

**Blindness:** Double blind

**Duration (days):** Mean 1423

**Setting:** 172 collaborating centers in 7 regions worldwide: Australia & NZ, China, France & Belgium, Italy, Japan, Sweden, UK and Republic of Ireland.

**Notes:** Mean follow-up of 3.9 years

**Info on Screening Process:** Not reported

#### Data Used

**MMSE**

**Diagnosis of dementia**

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 305</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Antihypertensive with - Flexible treatment regime based on perindopril 4mg/d with addition of indapamide 2.5mg/d for those whom the physician believe there was no specific indication for, nor contraindication to, the use of a diuretic. This was to maximise fall in blood pressure</td>
</tr>
<tr>
<td>Group 2</td>
<td>Placebo with - Identical in appearance to the active agents</td>
</tr>
</tbody>
</table>

#### Results from this paper:

**Internal Validity:**

1.1 Well covered
1.2 Adequately addressed
1.3 Not addressed
1.4 Poorly addressed
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 20% drop out
1.9 Not addressed
1.10 Not applicable

**Overall Assessment of the Study:**

2.1 -
2.2 Unsure
2.3 No
2.4 Yes

### Data Used

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td></td>
</tr>
<tr>
<td>Diagnosis of dementia</td>
<td></td>
</tr>
</tbody>
</table>

**Baseline:**

**Mean systolic blood pressure (mmHg):** 147

**Mean diastolic blood pressure (mmHg):** 86

**Age:** Mean 64

**Sex:** 4274 males 1831 females

**Exclusions:**

- No history of TIA or stroke within the last 5 years; insufficiently well to attend regular study clinics; subarachnoid haemorrhage (ischaemic stroke, haemorrhagic stroke, unknown pathological stroke all eligible).

**Normotensive and hypertensive patients were eligible for inclusion.**
### SCOPE2003

**Study Type:** RCT (individual)

**Study Description:** Investigator sent fax of patient data for central randomisation & received treatment allocation. Allocated by central computerised randomised schedule.

**Type of Analysis:** Intention to treat and last value carried forward

**Blindness:** Double blind

**Duration (days):** Range 1095-1825

**Setting:** 527 centres in 15 countries, mainly Europe.

**Info on Screening Process:** Not reported

**Data Used**
- **Major cardiovascular events**

<table>
<thead>
<tr>
<th>Group</th>
<th>N=</th>
<th>Antihypertensive with candesartan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>247</td>
<td>- Mean dose 11.6mg - Started with 8mg candesartan once daily in the morning. If SBP remained greater than 169mmHg, or decreased by less than 10mmHg, or DBP remained greater than 85mmHg, dose was doubled.</td>
</tr>
<tr>
<td>2</td>
<td>246</td>
<td>- Matching placebo, similar in appearance and taste.</td>
</tr>
</tbody>
</table>

**Info on Diagnosis:**
- **Age:** Mean 76
- **Sex:** 1780 males 3184 females
- **Exclusions:** Secondary hypertension; SBP>180mmHg; orthostatic hypotension; need of antihypertensive treatment other than HCT during the run-in period; stroke or myocardial infarction within 6 months; decompensated heart failure; serum aspartate aminotransferase or serum alanine aminotransferase >3 times above normal limit of the laboratory; serum creatinine > 180 umol/l in men and > 140 umol/l in women; contraindications for study drug or HCT; serious concomitant diseases affecting survival; and alcoholism or drug abuse.

**Notes:** No reported diagnosis

**Baseline:**
- Blood pressure (mmHg, mean): 166.0/90.3 Candesartan, 166.5/90.4 placebo
- MMSE (mean): 28.5 Candesartan, 28.5 placebo

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Well covered
- 1.3 Well covered
- 1.4 Well covered
- 1.5 Adequately addressed
- 1.6 Adequately addressed
- 1.7 Adequately addressed
- 1.8 0.24% treatment arm, 0.08% control arm
- 1.9 Well covered
- 1.10 Not addressed

**Overall Assessment of the Study**
- 2.1 1++
- 2.2
- 2.3 Unsure
- 2.4 Yes

### SCOTT2001

**Study Type:** Systematic Review

**Blindness:**

**Duration (days):**

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Not applicable
- 1.3 Well covered
**SHEP1991**

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Description:</strong> Multicenter study. Participants stratified by clinical center and by antihypertensive medication status at initial contact.</td>
</tr>
<tr>
<td><strong>Blindness:</strong> Double blind</td>
</tr>
<tr>
<td><strong>Duration (days):</strong> Mean 1642</td>
</tr>
<tr>
<td><strong>Setting:</strong> Community based ambulatory population in tertiary care centers.</td>
</tr>
<tr>
<td><strong>Info on Screening Process:</strong> 447 921 screened, 443 185 excluded. Reasons not given.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>n= 4736</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 72</td>
</tr>
<tr>
<td>Sex: 2046 males 2690 females</td>
</tr>
<tr>
<td>Diagnosis: No dementia</td>
</tr>
<tr>
<td>Exclusions: Systolic blood pressure off 220mmHg or more; major CVD such as recent MI or stroke; other major disease such as cancer, alcoholic liver disease or renal dysfunction; and presence of medical management problems such as clinically apparent depression or diabetes treated with insulin.</td>
</tr>
<tr>
<td>Baseline: Blood pressure mmHg, mean (SD): Systolic 170.3 (9.4), Diastolic 76.6 (9.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal and fatal stroke</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 1 N= 236</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensive with . Mean dose 25mg - Step 1, dose 1: chlorthalidone 12.5mg/day</td>
</tr>
<tr>
<td>Step 1, dose 2: chlorthalidone 25mg/day</td>
</tr>
<tr>
<td>Step 2, dose 1: atenolol 25mg/day</td>
</tr>
<tr>
<td>Step 2, dose 2: atenolol 50mg/day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2 N= 237</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo with - Matching placebo given in the same procedure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Results from this paper:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Validity:</td>
</tr>
<tr>
<td>1.1 Well covered</td>
</tr>
<tr>
<td>1.2 Poorly addressed</td>
</tr>
<tr>
<td>1.3 Not reported</td>
</tr>
<tr>
<td>1.4 Well covered</td>
</tr>
<tr>
<td>1.5 Adequately addressed</td>
</tr>
<tr>
<td>1.6 Adequately addressed</td>
</tr>
<tr>
<td>1.7 Well covered</td>
</tr>
<tr>
<td>1.8 After one year; 1% treatment group, 1.5% placebo</td>
</tr>
<tr>
<td>1.9 Not reported</td>
</tr>
<tr>
<td>1.10 Not reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Assessment of the Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 1-</td>
</tr>
<tr>
<td>2.2 Favoors treatment</td>
</tr>
<tr>
<td>2.3 No</td>
</tr>
<tr>
<td>2.4 Yes</td>
</tr>
</tbody>
</table>

---

**SHUMAKER2003**

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blindness:</strong> Double blind</td>
</tr>
<tr>
<td><strong>Duration (days):</strong></td>
</tr>
<tr>
<td><strong>Notes:</strong> 3 mth washout period prior to initial screening</td>
</tr>
<tr>
<td><strong>Info on Screening Process:</strong> 4894 screened; 362 withdrew consent 4532 enrolled and randomised</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>n= 4532</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
</tr>
<tr>
<td>Sex: all females</td>
</tr>
<tr>
<td>Diagnosis:</td>
</tr>
<tr>
<td>Exclusions: Persons not enrolled for WHI Hormone Therapy Trials; Age &lt;65 or diagnosis of probable dementia.</td>
</tr>
<tr>
<td>WHI exclusion criteria: Invasion cancer in past 10 years; history or suspicion of breast cancer; stroke/ischemic attack in past 6 mths;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 1 N= 222</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen plus progestin with . Mean dose 0.625mg + 2.5mg - 1 daily tablet containing conjugated equine estrogen (0.625mg) and medroxyprogesterone acetate (2.5mg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2 N= 230</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo with - Matching placebo taken once daily</td>
</tr>
</tbody>
</table>

---
**STANDRIDGE2004A**

**Study Type:** Systematic Review  
**Blindness:**  
**Duration (days):**

<table>
<thead>
<tr>
<th>Results from this paper:</th>
<th>Internal Validity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Well covered</td>
<td>1.1  Well covered</td>
</tr>
<tr>
<td>1.2 Adequately addressed</td>
<td>1.2 Adequately addressed</td>
</tr>
<tr>
<td>1.3 Adequately addressed</td>
<td>1.3 Adequately addressed</td>
</tr>
<tr>
<td>1.4 Adequately addressed</td>
<td>1.4 Adequately addressed</td>
</tr>
<tr>
<td>1.5 Adequately addressed</td>
<td>1.5 Adequately addressed</td>
</tr>
<tr>
<td>Overall assessment of the study:</td>
<td>2.1 +</td>
</tr>
<tr>
<td>2.2 N/A various interventions</td>
<td></td>
</tr>
</tbody>
</table>

**STYSEUR1999**

**Study Type:** RCT (individual)  
**Study Description:** After stratification by centre, sex and previous vascular complications, patients were randomised by means of a computerised random function.  
**Type of Analysis:** Intention to Treat and per-protocol analysis  
**Blindness:** Double blind  
**Duration (days):** Mean 730  
**Setting:** Enrolled at 106 centres from 19 European countries.  
**Info on Screening Process:** 3162 screened, n= 2418  
**Age:** Mean 70  
**Sex:** 829 males  1589 females  
**Diagnosis:** 100% No dementia  
**Exclusions:** Diagnosis of dementia, under 60 years of age, sitting systolic blood pressure not between 160-219mmHg with diastolic blood pressure over 95mmHg, standing systolic blood pressure under 140mmHg, no informed consent, not available for long term follow-up.

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Diagnosis of dementia MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td>N= 123</td>
</tr>
<tr>
<td>Antihypertensive with - Initiated with nitrendipine (10-40mg/day) with the poss addition of or replacement by enalapril (5-2 mg/day), hydrochlorothiazide or both drugs. Stepwise titrated &amp; combined to reduce sitting systolic blood pressure by 20mmHg or more to less than 150mmHg.</td>
<td></td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td>N= 118</td>
</tr>
<tr>
<td>Placebo with - Received matching placebo tablets.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Description:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 N= 123 Group</td>
<td>Antihypertensive with - Initiated with nitrendipine (10-40mg/day) with the poss addition of or replacement by enalapril (5-2 mg/day), hydrochlorothiazide or both drugs. Stepwise titrated &amp; combined to reduce sitting systolic blood pressure by 20mmHg or more to less than 150mmHg.</td>
</tr>
<tr>
<td>2 N= 118 Group</td>
<td>Placebo with - Received matching placebo tablets.</td>
</tr>
</tbody>
</table>
Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Adequately addressed
1.7 Well covered
1.8 After one year 1% (placebo), 1.4% (treatment)
1.9 Well covered
1.10 Not addressed

Overall Assessment of the Study:
2.1 1+
2.2 Increase the effect of treatment
2.3 No
2.4 Yes

SZEKELY2004
Study Type: Systematic Review

Blindness:
Duration (days):

Results from this paper:
Internal Validity:
1.1  Well covered
1.2 Well covered
1.3 Well covered
1.4 Adequately addressed
1.5 Adequately addressed

Overall assessment of the study:
2.1 +
2.2

UK-MRC1996
Study Type: RCT (individual)
Study Description: Cognitive sub-study within a RCT
Type of Analysis: Intention to treat
Blindness: Single blind
Duration (days):
Followup: 5.8 years (mean)
Setting: 226 general practices from the Medical Research Council’s general practice research framework.
Info on Screening Process: Screened 4396.

n= 2584
Age: Mean 70
Sex: 1085 males 1499 females

Exclusions: Taking antihypertensive medication; cardiac failure, angina, diabetes, asthma or other serious disease; myocardial infarction or cardiovascular accident in the previous 3 months; systolic pressure not within 160-209mmHg; mean diastolic pressure >115mmHg during eight week run in; not between the ages of 65-74.

Data Used
Trail making test
Paired associate learning test

Group 1 N= 633
Diuretic with . Mean dose 25mg/2.5mg - Hydrochlorothiazide 25mg plus amiloride 2.5mg daily

Group 2 N= 640
B Blocker with . Mean dose 50mg - Atenolol 50mg daily

Group 3 N= 131
Placebo with - Matching placebo
### VALENZUELA2005

**Study Type:** Systematic Review  
**Blindness:**  
**Duration (days):**

<table>
<thead>
<tr>
<th>Results from this paper:</th>
<th>Internal validity:</th>
<th>Overall assessment of the study:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.1 Well covered</td>
<td>2.1 +</td>
</tr>
<tr>
<td></td>
<td>1.2 Adequately addressed</td>
<td>2.2 Favours brain reserve as protective</td>
</tr>
<tr>
<td></td>
<td>1.3 Well covered</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4 Poorly addressed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5 Adequately addressed</td>
<td></td>
</tr>
</tbody>
</table>

### VISCOLI2002

**Study Type:** RCT (individual)  
**Study Description:** Secondary analysis for Women's Estrogen for Stroke Trial (WEST).  
**Blindness:** Double blind  
**Followup:** 5 mths  
**Setting:** USA  
**Notes:** Specifics reported elsewhere

<table>
<thead>
<tr>
<th>Data Used</th>
<th>MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 N= 231 Oestrogen (estradiol) with . Mean dose 1mg - Estradiol-17beta, standard dose, daily</td>
<td></td>
</tr>
<tr>
<td>Group 2 N= 230 Placebo with . Mean dose 1mg - Matching placebo</td>
<td></td>
</tr>
</tbody>
</table>

### WISNIEWSKI2002

<table>
<thead>
<tr>
<th>Results from this paper:</th>
<th>Internal Validity:</th>
<th>Overall Assessment of the Study:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.1 Well covered</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>1.2 Not reported</td>
<td>2.2 In favour of treatment</td>
</tr>
<tr>
<td></td>
<td>1.3 Not reported</td>
<td>2.3 No</td>
</tr>
<tr>
<td></td>
<td>1.4 Well covered</td>
<td>2.4 Yes</td>
</tr>
<tr>
<td></td>
<td>1.5 Adequately addressed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.6 Adequately addressed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.7 Well covered</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.9 Not reported</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.10 Not reported</td>
<td></td>
</tr>
</tbody>
</table>

| Diagnosis: | Age: Mean 70 Range 46-90  
Sex: all females  
Exclusions: All except postmenopausal women with nondisabling stroke or transient ischemic attack in past 3 months; Specifics reported elsewhere  
Notes: 39% had Center for Epidemiologic Studies of Depression (CES-D) scores compatible with depression at entry |
Baseline: Estradiol group: MMSE = 26.9  
Placebo group: MMSE = 27.1 |

### WISNIEWSKI2002

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: Predetermined randomisation code unknown to experimenters or participants. No further details about how identity of medication masked.</td>
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<tr>
<td>Blindness: Double blind</td>
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<td>Duration (days): Mean 120</td>
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<td>Setting: USA</td>
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<td>Info on Screening Process: 26 enrolled</td>
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**Data Used**

<table>
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<tr>
<th>Factor-Reference Cognitive Tests</th>
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**Group 1**

- **N = 13**
- Oestrogen with. Mean dose 1.25mg - Oral esterified estrogen (E group) daily for 4 mths

**Group 2**

- **N = 13**
- Oestrogen with. Mean dose 1.25mg - Oral esterified estrogen for 4 mths
- Testosterone with. Mean dose 2.5mg - Oral methyltestosterone daily for 4 mths

**Results from this paper:**

**Internal Validity:**

| 1.1 Well covered |
| 1.2 Adequately addressed |
| 1.3 Not reported |
| 1.4 Well covered |
| 1.5 Well covered |
| 1.6 Well covered |
| 1.7 Adequately addressed |
| 1.8 |
| 1.9 Not addressed |
| 1.10 Not applicable |

**Overall Assessment of the Study:**

| 2.1 In favour of treatment |
| 2.2 No |
| 2.3 No |
| 2.4 Yes |

### YAFFE2005

<table>
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<tr>
<th>Study Type: RCT (cluster)</th>
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<tbody>
<tr>
<td>Study Description: Randomly assigned by site</td>
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<tr>
<td>Type of Analysis: Intention to treat</td>
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<tr>
<td>Blindness: No mention</td>
</tr>
<tr>
<td>Duration (days):</td>
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<tr>
<td>Followup: 3 years</td>
</tr>
<tr>
<td>Setting: 180 clinical sites in 25 countries</td>
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<td>Info on Screening Process: No details given here</td>
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**Data Used**

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<tr>
<th>Diagnosis of dementia</th>
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**Group 1**

- **N = 179**
- Raloxifene with. Mean dose 60mg/day - All asked to also take calcium (500mg) and vitamin D (400-600 IU) daily

**Group 2**

- **N = 182**
- Raloxifene with. Mean dose 120mg/day - All asked to also take calcium (500mg) and vitamin D (400-600 IU) daily

**Group 3**

- **N = 176**
- Placebo with. Identical placebo. All asked to also take calcium (500mg) and vitamin D (400-600 IU) daily
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<td>ABYAD2002</td>
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<tr>
<td>AISEN2003</td>
<td>Not prevention</td>
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<tr>
<td>BELL1992</td>
<td>not required intervention - antidepressants + vitamins</td>
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<tr>
<td>BLASS1988</td>
<td>Not prevention</td>
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<tr>
<td>BROUWER2000</td>
<td>did not fulfill participant criteria</td>
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<tr>
<td>CARLSSON2002</td>
<td>Not vitamin E alone</td>
</tr>
<tr>
<td>CARNEY1976</td>
<td>Not required intervention</td>
</tr>
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<td>CHANDRA2001</td>
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<td>CHERUBIN12005</td>
<td>not intervention</td>
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<td>COCKLE2000</td>
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<td>DEJONG2001</td>
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<td>DELAFOURNIERE1997</td>
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<td>EASTLEY2000</td>
<td>Not RCT</td>
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<tr>
<td>FEIGIN2005</td>
<td>Non RCT, meta-analysis</td>
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<td>FORREST1960</td>
<td>Did not fulfill participant criteria</td>
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<tr>
<td>HUGHES1970</td>
<td>No measure of cognitive function</td>
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<td>KANOFSKY1996</td>
<td>Not primary level study</td>
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<td>KLATTE2003</td>
<td>Not prevention</td>
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<td>LEBLHUBER2004</td>
<td>Not prevention</td>
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<td>MAGNUS1974</td>
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<td>MARTIN1992</td>
<td>No control group</td>
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<tr>
<td>MEADOR1993A</td>
<td>Not prevention</td>
</tr>
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<td>MIMORI1996</td>
<td>Not prevention</td>
</tr>
<tr>
<td>MOFFAT2000</td>
<td>Not prevention</td>
</tr>
<tr>
<td>MURRAY2002</td>
<td>Non RCT, longitudinal analysis</td>
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<tr>
<td>NAGGA2002</td>
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<td>NOLAN1991</td>
<td>Not prevention</td>
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<tr>
<td>ONOFRIJ2002</td>
<td>Not prevention</td>
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<tr>
<td>ONOFRIJ2003</td>
<td>Not prevention</td>
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<tr>
<td>PASSERI1993</td>
<td>Not prevention</td>
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<td>PERRIG1997</td>
<td>Not intervention</td>
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<td>ROGERS1993</td>
<td>Not prevention</td>
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<td>SANO1996</td>
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<td>SANO1996A</td>
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<tr>
<td>SANO1997A</td>
<td>Not prevention</td>
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<td>SEAL2002</td>
<td>Included in Malouf (2003) cochrane review of Vitamin B12 for cognition</td>
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<tr>
<td>SOBOW2003</td>
<td>Not prevention</td>
</tr>
<tr>
<td>SOMMER2003</td>
<td>Not prevention</td>
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<tr>
<td>TAKAO2001</td>
<td>Not prevention</td>
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<tr>
<td>TEUNISSE1996</td>
<td>Not prevention</td>
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References of Included Studies

**BAGGER2005** (Published Data Only)

**BARNHART1999** (Published Data Only)

**BRYAN2002** (Published Data Only)

**CLARKE2003** (Published Data Only)

**DECAEN2005** (Published Data Only)

**ETMINAN2003** (Published Data Only)

**FIO RAV ANTI1997** (Published Data Only)

**GARCIA2004** (Published Data Only)

**GRADY2002** (Published Data Only)

**HENDERSON2005** (Published Data Only)

**HOPE2002** (Published Data Only)

**HUPPERT2000** (Published Data Only)

**HVAS2004** (Published Data Only)

**WANG2002A** Non RCT, prospective cohort study

**WOLF1997** Did not fulfill participant criteria

**WOLF1997A** No data for time of cross-over

**WOLF1998** Not prevention of dementia

**WOLKOWITZ2003** Not prevention

**WOUTERSWESSELIN2002** Not required intervention

**ZEC2002** Non-systematic review
IN'TVELD2001

KWOK1998

LOW2005

MALOUF2005

MALOUF2003A

MILLER2005

MORRIS2005

PAN2003

PROGRESS2003

SCOPE2003

SCOTT2001
References of Excluded Studies

**SHEP1991 (Published Data Only)**


**SHUMAKER2003 (Published Data Only)**

**STANDRIDGE2004A (Published Data Only)**

*Prevention of isolated systolic hypertension and dementia prevention in older patients. Results of the Systolic Hypertension in Europe trial (SYST-EUR) vascular dementia project. European Heart Journal Supplements., 1.*

**SYST-EUR1999 (Published Data Only)**


**SZEKELY2004 (Published Data Only)**

**UK-MRC1996 (Published Data Only)**

**VALENZUELA2005 (Published Data Only)**

**VISCOLI2002 (Published Data Only)**

**WISNIEWSKI2002 (Published Data Only)**

**YAFFE2005 (Published Data Only)**
ABYAD2002 (Published Data Only)

AISEN2003 (Published Data Only)

BELL1992 (Published Data Only)

BLASS1988 (Published Data Only)

BROUWER2000 (Published Data Only)

CARLSSON2002 (Published Data Only)

CARNEY1976 (Published Data Only)

CHANDRA2001 (Published Data Only)

CHERUBINI2005 (Published Data Only)

COCKLE2000 (Published Data Only)

DEJONG2001 (Published Data Only)

DELAFOURNIERE1997 (Published Data Only)

EASTLEY2000 (Published Data Only)

FEIGIN2005 (Published Data Only)

FEIGIN2005 (Published Data Only)

FORREST1960 (Published Data Only)

HUGHES1970 (Published Data Only)
KANOFSKY1996 (Published Data Only)

KLATTE2003 (Published Data Only)

LEBLHUBER2004 (Published Data Only)

MAGNUS1974 (Published Data Only)

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MIMORI1996 (Published Data Only)

MOFFAT2000 (Published Data Only)

MURRAY2002 (Published Data Only)

NAGGA2002 (Published Data Only)

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ONOFRI2002 (Published Data Only)

ONOFRI2003 (Published Data Only)

PASSERI1993 (Published Data Only)

PERRIG1997 (Published Data Only)

ROGERS1993 (Published Data Only)

SANO1996 (Published Data Only)

SANO1996A

SANO1997

SANO1997A

SEAL2002

SOBOW2003

SOMMER2003

TAKAO2001

TEUNISSE1996

VANNIEKERK2001

WANG2002A

WOLF1997

WOLF1997A

WOLF1998


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Table 2: Included studies table for review of diagnostic test accuracy

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<tr>
<th>Bibliographic reference</th>
<th>Study type</th>
<th>Evidence level</th>
<th>Number of patients (or studies)</th>
<th>Prevalence</th>
<th>Patient characteristic(s)</th>
<th>Type of test*</th>
<th>Reference standard</th>
<th>Sensitivity and specificity</th>
<th>Positive and negative predictive value</th>
<th>Source of funding/ additional comments</th>
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<tr>
<td>[1]</td>
<td>Review</td>
<td>Class I (3 studies)</td>
<td>13 studies</td>
<td>Dementia: 5% of the over 65 yr olds; 20% of over 80 yr olds (of these, 60% have AD)</td>
<td>DAT or probable AD</td>
<td>DSM-III-R or NINCDS/ADRDA</td>
<td>Neuropathologic confirmation</td>
<td>Mean sensitivity = 81% (range 49-100%) Mean specificity = 70% (range 47-100%)</td>
<td>American Academy of Neurology</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Class II (10 studies)*</td>
<td>4 studies</td>
<td>See Riedel-Heller 2006 for latest review</td>
<td>Possible AD</td>
<td>NINCDS/ADRDA</td>
<td>Neuropathologic confirmation</td>
<td>Mean sensitivity = 93% (range 85-96%) Mean specificity = 48% (range 32-61%)</td>
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<tr>
<td>Class I</td>
<td>1 study</td>
<td>Dementia: 5% of the over 65 yr olds; 20% of over 80 yr olds (of these, 15-20% have VaD)</td>
<td>VaD</td>
<td>NINDS-AIREN</td>
<td>Neuropathologic confirmation</td>
<td>Mean sensitivity = 43% Mean specificity = 95%</td>
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<tr>
<td>Class I</td>
<td>1 study</td>
<td>Dementia: 5% of the over 65 yr olds; 20% of over 80 yr olds (of these, 15-20% have DLB)</td>
<td>DLB</td>
<td>DLB criteria</td>
<td>Sensitivity = 22% Specificity = 100%</td>
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<td>Class II</td>
<td>5 studies</td>
<td>DLB</td>
<td>DLB criteria</td>
<td>Mean sensitivity = 58% (range 34-75%) Mean specificity = 95%</td>
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<td>Author(s)</td>
<td>Methodology</td>
<td>Sample Size</td>
<td>Diagnosis</td>
<td>Diagnostic Criteria</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Positive Predictive Value (PPV)</td>
<td>Negative Predictive Value (NPV)</td>
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<tr>
<td>Gold et al., 2002</td>
<td>Autopsy case study</td>
<td>89</td>
<td>VaD, AD or mixed dementia</td>
<td>DSM-IV Neuropathologic confirmation</td>
<td>Sensitivity = 50%</td>
<td>Specificity = 84%</td>
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<td>Gold et al., 2002</td>
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<td>ADDTC possible/probable</td>
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<td>Sensitivity = 70/25%</td>
<td>Specificity = 78/91%</td>
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<td>Gold et al., 2002</td>
<td></td>
<td></td>
<td>NINDS-AIREN possible/probable</td>
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<td>Sensitivity = 55/20%</td>
<td>Specificity = 84/93%</td>
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<td>Gold et al., 2002</td>
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<td>ICD-10</td>
<td></td>
<td>Sensitivity = 20%</td>
<td>Specificity = 94%</td>
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<td>Litvan et al., 2003</td>
<td>Review</td>
<td>?</td>
<td>2 studies</td>
<td>Possible DLB Consensus diagnostic criteria</td>
<td>Varied</td>
<td>Mean sensitivity = 95% (range = 89-100%)</td>
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<td></td>
<td></td>
<td>?</td>
<td>7 studies</td>
<td>Probable DLB Consensus diagnostic criteria</td>
<td>Varied</td>
<td>Mean specificity = 14% (range = 0-28%)</td>
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<td>Dougall et al., 2004</td>
<td>Review</td>
<td>8 case control studies</td>
<td>AD vs. VaD HMPAO SPECT</td>
<td>Varied</td>
<td>Mean sensitivity = 49% (range = 0-83%)</td>
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In part from National Institute on Aging.
<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Methodology</th>
<th>Number of studies</th>
<th>Conclusion</th>
<th>Imaging Method</th>
<th>Imaging Results</th>
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<td>Patwardhan et al., 2004</td>
<td>Review</td>
<td>Varied</td>
<td>9 studies</td>
<td>AD vs. healthy controls</td>
<td>PET</td>
<td>Pooled weighted sensitivity = 86% (95% CI 76-93) Pooled weighted specificity = 86% (95% CI 72-93)</td>
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<td>Mosconi, 2005</td>
<td>Review</td>
<td>?</td>
<td>1 study</td>
<td>DLB vs. AD</td>
<td>PET</td>
<td>Neuropathologic confirmation Sensitivity = 90% Specificity = 80%</td>
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<td>1 study</td>
<td>AD vs. VaD</td>
<td>PET</td>
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<td>AD vs. MDD</td>
<td>PET</td>
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<td>Study Type</td>
<td>Tools Used</td>
<td>Diagnosis Method</td>
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<td>Bacchetta et al., 2006</td>
<td>Case series</td>
<td>ADDTC, NINDS-AIREN, HIS, Autopsy</td>
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<td>Oksengard &amp; Winblad, 2004</td>
<td>Review</td>
<td>Various cognitive assessment tools</td>
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<td>De Jager et al., 2003</td>
<td>Case-control</td>
<td>Various neuropsychological tests</td>
<td>Consensus diagnosis by two experienced clinicians based on clinical history and examination, neuroradiological findings and results on CAMDEX</td>
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<td>Moroney et al., 1997</td>
<td>Review</td>
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<td>Lorentz et al., 2002</td>
<td>Review</td>
<td>Various brief screening tests</td>
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<td>Kuslansky et al., 2004</td>
<td>Cohort study</td>
<td>Hopkins Verbal Learning Test, MMSE</td>
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<td>Andreasen &amp; Blennow, 2004</td>
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<td>Biological markers</td>
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<td>Wiltfang et al., 2005</td>
<td>Cohort study?</td>
<td>N=2808</td>
<td>Analysis stratified for age (&lt;65, 65-80 and &gt;80 years), gender, education (&lt;6 or &gt;5 years) and presence of congestive heart failure (CHF)</td>
<td>Abbreviated Mental Test (AMT)</td>
<td>Diagnosis of dementia made according to DSM-III-R criteria</td>
<td>Sensitivity (81%), Specificity (84%)</td>
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<tr>
<td>Antonelli et al., 2003</td>
<td>Cohort study?</td>
<td>N=220</td>
<td>Aged 40-80 yrs, diagnosis of parkinsonism or essential tremor. Patients with evidence of cerebrovascular disease, other structural brain disease, dementia, head injury, or encephalitis were excluded.</td>
<td>72% parkinsonism, 12% essential tremor, 16% healthy volunteers</td>
<td>63 yrs (mean), 60% male</td>
<td>SPECT</td>
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<tr>
<td>Benamer et al., 2000</td>
<td>Cohort study?</td>
<td>N=220</td>
<td>Incl if &gt;74 yrs of age</td>
<td>82/283 diagnosis of dementia</td>
<td>Mean age 79.6 yrs,</td>
<td>GPCOG</td>
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<tr>
<td>Brodaty et al., 2002</td>
<td>Cohort study?</td>
<td>N=283</td>
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<td>N</td>
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<td>Cognitive Tests</td>
<td>Diagnostic Criteria</td>
<td>Results</td>
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<tr>
<td>Brooke et al., 1999</td>
<td>Cohort study</td>
<td>287</td>
<td>152 with diagnosis of dementia; 135 controls; 33% male; mean age 75 yrs</td>
<td>MMSE, AMT</td>
<td>GDS</td>
<td>6 Item Cognitive Impairment Test (6CIT)</td>
</tr>
</tbody>
</table>

MMSE DSM-IV 81% sensitivity; 76% specificity
Positive predictive value 57% Negative predictive value 90%

AMT DSM-IV 42% sensitivity; 93% specificity
Positive predictive value 71% Negative predictive value 80%

6CIT GDS
Conventional cutoff 23/24 sensitivity 51.43%, specificity 100%; higher cutoff 25/26 sensitivity 64.29%, specificity 100%

Positive predictive value 67% Negative predictive value 92%

Regardless of cog. Status. Excl if resided in nursing home, diagnosis of depression or delirium, poor english skills.

40.6% male, 87.6% lived in a private home.

Health and family services general practice evaluation program.
<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Study</th>
<th>N</th>
<th>Diagnosis Details</th>
<th>Mean Age</th>
<th>Imaging Method</th>
<th>ICD-10 Description</th>
<th>Sensitivity/Specificity</th>
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<tbody>
<tr>
<td>Hentschel et al., 2005</td>
<td>Cohort study?</td>
<td>N=100</td>
<td>55 diagnosis of dementia</td>
<td>Mean age 68.6 yrs</td>
<td>MRI</td>
<td>ICD-10</td>
<td>Sensitivity: 55% (no dementia XD); 90% (vascular VD); 93% (neurodegenerative ND); Specificity: 90% XD; 83% VD; 90% ND</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>(100) subjects named dementia</td>
<td></td>
<td></td>
<td></td>
<td>Positive predictive value: 93% XD; 51% VD; 78% ND</td>
</tr>
<tr>
<td>Kim et al., 2005</td>
<td>Cohort study?</td>
<td>N=164</td>
<td>Excluding&lt; 50 yrs, non Korean speaking; inadequate hearing or vision; illiteracy; serious medical disorders.</td>
<td>Mean age 73 yrs; 63% female; mean education years 5</td>
<td>MMSE</td>
<td>DSM-IV; NINCDS-ADRDA</td>
<td>Sensitivity 98% XD; 60% VD; 83% ND Specificity 98% XD; 94% VD; 88% ND</td>
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<td>Hsich et al., 1996</td>
<td>Cohort study?</td>
<td>N=257</td>
<td>71 CJD; 186 healthy controls</td>
<td></td>
<td></td>
<td></td>
<td>Sensitivity 96%; Specificity 99%</td>
</tr>
<tr>
<td>Jagust et al., 2001</td>
<td>Cohort study?</td>
<td>N=155</td>
<td>Incl. cognitive loss acc.</td>
<td>Mean age 77 yrs; 46% male</td>
<td>SPECT</td>
<td>Autopsy</td>
<td>Sensitivity 63%; Specificity 93%</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Cohort Study?</td>
<td>N</td>
<td>Disease Description</td>
<td>Assessment</td>
<td>Diagnosis Criteria</td>
<td>Outcome</td>
</tr>
<tr>
<td>-------</td>
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<td>------------</td>
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<td>---------</td>
</tr>
<tr>
<td>Mathuranath et al., 2000</td>
<td>Cohort study?</td>
<td>N =139 Incl. follow-up of at least 12 months; able to complete full assessment; Excl. evidence of two or more pathologies; major depression (DSMIV) or other psychiatric illness; causes of cognitive impairment other than degenerative or vascular pathology</td>
<td>Dementia (n = 115); non-dementia (n = 24)</td>
<td>Mean age 65 yrs; 58% male</td>
<td>Addenbrooke's Cognitive Examination (ACE)</td>
<td>DSM-IV; NINCDS-ADRDA; NINDS-AIREN; consensus criteria for FTD</td>
<td>Positive predictive value 78%; Negative predictive value 86%</td>
</tr>
<tr>
<td>McKeith et al., 2000</td>
<td>Cohort study</td>
<td>N=50</td>
<td>DLB n=29; AD n=15; VaD n=5; one case had</td>
<td>Mean age at death 80 yrs; DLB</td>
<td>DLB International</td>
<td>Autopsy</td>
<td>Cut off score 83: sensitivity 82%; specificity 96%</td>
</tr>
</tbody>
</table>
### Abstract only

#### O'Brien et al., 2004
- Cohort study
- N=164 Healthy controls n=33; NINCDS/ADRDA confirmed AD n=34; consensus DLB n=23, PD n=38; PDD n=36
- SPECT NINCDS/ADRDA; DLB consensus diagnosis
- Distinguish between DLB and AD; sensitivity 78%; specificity 94%
- Distinguish between DLB and AD; positive predictive value 90%

#### Meulen et al., 2004
- Cohort study? N=587 AD n=177; other dementia n=164
- Seven minute screen
- AD sensitivity 92.9%; specificity 93.5%; Other dementia sensitivity 89.4%; specificity 93.5%

#### Orrell et al., 1992
- Cohort study? N=164 AD n=40 (24.4%); Multi-infarct dementia n=17; other dementia n=14; delirium n=3; depression n=63; mania n=2; paraphrenia n=11; other functional disorders n=9; no specified disorder n=6
- Felix Post Unit Questionnaire (FPU)-a test of memory and orientation
- DSM-III-R Differentiating between organic and functional disorders; sensitivity 84%; specificity 74%
- Differentiating between dementia and depressive disorders; sensitivity 85%; specificity 75%

---

**atypical pathologic features of progressive supranuclear palsy (PSP)***

| 58% female; AD 68% female; VaD 60% female |
| Consensus criteria |
| specificity 95% |

For a diagnosis of probable DLB:

- PPV 96%; NPV 80%
<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>77%</td>
<td>75%</td>
</tr>
<tr>
<td>Medical Research Council (MRC) score</td>
<td>Differentiating between organic and functional disorders; sensitivity 89%; specificity 57%. Differentiating between dementia and depressive disorders; sensitivity 90%; specificity 65%.</td>
<td></td>
</tr>
<tr>
<td>Cognitive Assessment Schedule (CASCH)</td>
<td>Differentiating between organic and functional disorders; sensitivity 71%; specificity 83%. Differentiating between dementia and depressive disorders; sensitivity 74%; specificity 86%.</td>
<td></td>
</tr>
</tbody>
</table>

White et al., 2002
Cohort study?
N=202 14% dementia 36% male; 54% of MMSE GMS–AGECAT ? False positive rate
### Additional studies not assessed:

- Bucks1996 – assessment of ADL not diagnostic test
- Ceravolo2004 – Not diagnostic accuracy
- Chui1997 – Not a specific test
- Hachinski1975 – Abstract only, sensitivity and specificity not reported
- Huppert1995 – Abstract only, sensitivity and specificity not reported
- Jack1999 – Prediction of progression from MCI to AD
- Jorm1989 – Abstract only, sensitivity and specificity not reported
- Klunk2004 – Sensitivity and specificity not reported
- MRC-CFAS – Not diagnostic accuracy
- Rosen 1984 – Abstract only, sensitivity and specificity not reported
- Rosen 1980 – Abstract only, sensitivity and specificity not reported
- Scahill 2002 – not diagnostic accuracy
- Stoub2005 – Predicting risk of AD
- Sunderland 1989 – Abstract only, sensitivity and specificity not reported
- Walker 2000 – Doesn’t report the accuracy of a diagnostic test
- Walker 2002 - sensitivity and specificity etc not reported
Williams 2003 - sensitivity and specificity etc not reported.

* Class I = Evidence provided by a well designed prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, in which test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy; Class II = Evidence provided by a well designed prospective study of a narrow spectrum of persons with the suspected condition, or a well designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared with a broad spectrum of controls, in which test is applied in blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type: observational, cohort, case studies, etc.</td>
</tr>
<tr>
<td>Evidence level: classified using levels of evidence for studies of diagnostic test accuracy.</td>
</tr>
<tr>
<td>Number of patients: total number of patients included in the study, with inclusion/exclusion criteria.</td>
</tr>
<tr>
<td>Prevalence: proportion of people with the disease in the population at risk.</td>
</tr>
<tr>
<td>Patient characteristics: relevant characteristics to the area of interest: age, sex, ethnic origin, comorbidity, disease status, community/hospital based.</td>
</tr>
<tr>
<td>Type of test: description of the test used in the study. *Specify the test threshold where applicable.</td>
</tr>
<tr>
<td>Reference standard: reference standard used as measure of outcome. Specify if it is a ‘gold’ standard or ‘current best practice’.</td>
</tr>
<tr>
<td>Sensitivity: proportion of individuals classified as positive by the gold (or reference) standard, who are correctly identified by the study test. Specificity: proportion of individuals classified as negative by the gold (or reference) standard, who are correctly identified by the study test.</td>
</tr>
<tr>
<td>Positive predictive value: proportion of individuals with a positive test result who actually have the disease. Negative predictive value: proportion of individuals with a negative test result who do NOT have the disease.</td>
</tr>
<tr>
<td>Source of funding: government funding (for example, NHS), voluntary/charity (for example, Wellcome Trust), pharmaceutical company.</td>
</tr>
<tr>
<td>Additional comments: additional characteristics/interpretations of the studies. Important flaws in the study not identifiable from other data in the table. A range of additional questions or issues that will need to be considered, but do not figure in the results table – for example, if a test is one of a sequence of tests, if its utility was determined.</td>
</tr>
</tbody>
</table>

**References**


Dementia Guideline Appendices May 2006


### Table 3: Included/excluded studies table for review of strategies for promoting independence

#### Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Exercise vs Conversation vs Exercise + Conversation</th>
<th>Falls prevention vs standard care</th>
<th>Occupational Therapy vs standard care</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAPPEN2000</td>
<td>JENSEN2003</td>
<td>DOOLEY2004</td>
</tr>
<tr>
<td></td>
<td>KELLY2002</td>
<td>JOSEPHSSON1995</td>
</tr>
<tr>
<td></td>
<td>SHAW2003A</td>
<td></td>
</tr>
</tbody>
</table>

#### Physical Exercise vs Active Control

|--------------|------------|---------------|---------------|------------|

#### Physical Exercise vs standard care

|--------------|----------|--------------|---------------|------------|--------------|-------------|------------|----------|----------|

#### Physical exercise vs wait-list control

<table>
<thead>
<tr>
<th>CHANDLER1998</th>
<th>TOULOTTE2003</th>
</tr>
</thead>
</table>

#### Specific technological devices vs standard care

<table>
<thead>
<tr>
<th>MIHAILEDIS2001</th>
</tr>
</thead>
</table>

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### Characteristics of Included Studies

#### Methods

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: Single blind</td>
</tr>
<tr>
<td>Duration (days): Mean 210</td>
</tr>
<tr>
<td>Setting: Nursing home residents in rural upstate New York</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timed Manual Performance</td>
</tr>
</tbody>
</table>

#### Participants

<table>
<thead>
<tr>
<th>n = 66</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 86</td>
</tr>
<tr>
<td>Sex: 8 males 58 females</td>
</tr>
<tr>
<td>Diagnosis:</td>
</tr>
<tr>
<td>Exclusions: Tacrine use, in the home for less than 3 months</td>
</tr>
<tr>
<td>Baseline: MMSE = 7.5</td>
</tr>
</tbody>
</table>

#### Interventions

<table>
<thead>
<tr>
<th>Group 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 33</td>
</tr>
<tr>
<td>Exercise with Every part of the day considered part of the program including handwashing, walking to meals, dressing, exercise, cognitive games and sensorimotor activities-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 33</td>
</tr>
<tr>
<td>Standard Care with The regular schedule of the nursing home activities and standard nursing care</td>
</tr>
</tbody>
</table>

#### Notes

<table>
<thead>
<tr>
<th>Results from this paper:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Validity:</td>
</tr>
<tr>
<td>1.1 Adequately addressed</td>
</tr>
<tr>
<td>1.2 Adequately addressed</td>
</tr>
<tr>
<td>1.3 Not addressed</td>
</tr>
<tr>
<td>1.4 Adequately addressed</td>
</tr>
<tr>
<td>1.5 Adequately addressed</td>
</tr>
<tr>
<td>1.6 Adequately addressed</td>
</tr>
<tr>
<td>1.7 Adequately addressed</td>
</tr>
<tr>
<td>1.8</td>
</tr>
<tr>
<td>1.9 Not reported</td>
</tr>
<tr>
<td>1.10 Not applicable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Assessment of the Study:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 1+</td>
</tr>
<tr>
<td>2.2 favours treatment</td>
</tr>
<tr>
<td>2.3 yes</td>
</tr>
<tr>
<td>2.4 yes</td>
</tr>
</tbody>
</table>
### CHANDLER1998

**Study Type:** RCT (individual)

- **Blindness:** No mention
- **Duration (days):** Mean 70

**Setting:** Community dwelling volunteers within a 25 mile radius of Durham Veteran Affairs Medical Center, US

- **Info on Screening Process:** 850 screened, 178 excluded on medical grounds, 241 too fit, 202 not interested, 129 excluded for other reasons
- 100 randomized, 13 dropped out - illness (9), death (1), loss of interest (1), unwillingness to undergo strength training (1)

**Diagnosis:**
- Age: Mean 78
- Sex: 50 males 50 females
- **Exclusions:** Too fit (Reuben's Advanced Activities of Daily Living) >3, terminal illness, severe unstable cardiac disease, severe fixed or progressive neurologic disease, complete blindness, lower extremity amputation, MMSE <18 and unable to follow 3-step command, able to descend stairs without using railing

**Baseline:** MMSE = 24.3

**Data Used**
- Six minute walk

**Group 1 N= 50**
- Exercise with - 3 sessions per week in home program of resistive lower extremity exercises using threadband and body weight resistance. Exercises included resisted hip extension and abduction, knee flexion and extension, ankle dorsiflexion, toe raises, chair raises.

**Results from this paper:**
- **Internal Validity:**
  1.1 Well covered
  1.2 Adequately addressed
  1.3 Not reported
  1.4 Not addressed
  1.5 Adequately addressed
  1.6 Adequately addressed
  1.7 Adequately addressed
  1.8 13% dropped out
  1.9 Not addressed
  1.10 Not addressed

- **Overall Assessment of the Study:**
  2.1 1+
  2.2 favours treatment
  2.3 yes
  2.4 MMSE = 24

### COTT2002

**Study Type:** RCT (individual)

**Study Description:** P's randomised into walking/talking prog, talking prog or control group and measured effect on functional status. No info on how they were randomised.

- **Blindness:** No mention
- **Duration (days):** Mean 112

**Setting:** 3 geriatric long-term care facilities in Metropolitan Toronto.

- **Info on Screening Process:** 103 screened 17 excluded

**Diagnosis:**
- Age: Mean 82
- Sex: 35 males 39 females
- **Exclusions:** no medical diagnosis of AD, >20 MMSE, cardiac conditions that would preclude ambulation, score of >3 on item 8 of MMSE, inability to walk 5m with or without an assistive device or supervision.

**Baseline:** MMSE = 6

**Data Used**
- London Psychogeriatric Rating Scale
- Functional Assessment of Communication Skills
- 2-min walk test

**Group 1 N= 30**
- Combined intervention with - Walk and Talk: Received conversation while walking in pairs. 30 minute session, 5 times a week, over 16 weeks. Done in corridors of the residents' units and consisted of supervised walking in pairs.

**Group 2 N= 25**
- Behavioural with - Talk only: Received conversation while sitting in pairs with a Research Assistant for 30 minutes, 5 times a week for the 16 week intervention period.

**Group 3 N= 19**
- No treatment with - Received only pre and post measures of the outcome variables.

### DOOLEY2004

**Study Type:** RCT (individual)

**Study Description:** Pretest-posttest control group design.

- **n= 40**
- **Age:** Mean 77
- **Sex:** 16 males 24 females

**Data Used**
- PSMS
- AAL-AD
- Zarit Burden Interview

**Group 1 N= 20**
- Occupational therapy with - Registered occupational therapist administered the Assessment of Instrumental Function and wrote a report providing
### FRANCESE1997

**Study Type:** RCT (individual)

- **Blindness:** No mention
- **Duration (days):** Mean 49
- **Setting:** 60 bed Alzheimer unit in a Medicare nursing facility in North Virginia

<table>
<thead>
<tr>
<th>Group</th>
<th>Study Type</th>
<th>Setting</th>
<th>Duration (days)</th>
<th>Blindness</th>
<th>Diagnosis</th>
<th>Exclusions</th>
<th>Data Used</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1N = 12</td>
<td>Exercise with</td>
<td>- For 20 mins in the morning three times a week for 7 weeks incorporating the use of music, canes (for hand grips), bean bags, beach balls, velcro ball and mitt as well as parachute leg weights</td>
<td>60 bed Alzheimer unit in a Medicare nursing facility in North Virginia</td>
<td>Mean 49</td>
<td>Age:</td>
<td>No understanding of English language, medically unfit (e.g. severe arthritic or contracture conditions), doesn't need the assistance of carers.</td>
<td>Tinetti Balance, CADS</td>
<td>AMPS - performing daily activities IDDD - initiative and need for assistance in performing daily activities</td>
</tr>
</tbody>
</table>

**Results from this paper:**

<table>
<thead>
<tr>
<th>Internal Validity:</th>
<th>1.1 Well covered</th>
<th>1.2 Not reported</th>
<th>1.3 Not addressed</th>
<th>1.4 Not addressed</th>
<th>1.5 Adequately addressed</th>
<th>1.6 Adequately addressed</th>
<th>1.7 Adequately addressed</th>
<th>1.8 8.3% drop out</th>
<th>1.9 Not addressed</th>
<th>1.10 Not applicable</th>
</tr>
</thead>
</table>

**Overall Assessment of the Study:**

2.1 1+  
2.2 favours treatment  
2.3 yes  
2.4 yes

### GRAFF2003

**Study Type:** Before-After study/Interrupted time series

- **Blindness:**
- **Duration (days):** Mean 35
- **Setting:** older individual with cognitive impairment who were to be discharged to their homes or residential home

<table>
<thead>
<tr>
<th>Group</th>
<th>Study Type</th>
<th>Setting</th>
<th>Duration (days)</th>
<th>Blindness</th>
<th>Diagnosis</th>
<th>Exclusions</th>
<th>Data Used</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1N = 12</td>
<td>Occupational Therapy with</td>
<td>- Received OT intervention twice a week for 2 weeks in hospital and twice a week for 5 weeks at home. Approach was client-based and environmentally/psychosocially based. Included participant and their primary carer</td>
<td>older individual with cognitive impairment who were to be discharged to their homes or residential home</td>
<td>Mean 35</td>
<td>Age: Mean 80</td>
<td>young people, MMSE &lt;10 &gt;24, Cambridge Cognitive Screening Test &gt;78/80, cognitive impairment and depression/moderate psychiatric disorder, should be admitted to a nursing home, absence of occupational therapy recommendations and reviewed with the caregiver during a home visit. Follow-up and assessment 1-6 months later.</td>
<td>IDDD, AMPS</td>
<td>IDDD - initiative and need for assistance in performing daily activities AMPS - performing daily activities</td>
</tr>
</tbody>
</table>

### Summary

- **Group 2 N= 20**
  - No treatment with - Registered occupational therapist administered the Assessment of Instrumental Function and wrote a report providing occupational therapy recommendations, not given until after the follow-up assessments 1-6 months later.

<table>
<thead>
<tr>
<th>Group</th>
<th>Setting</th>
<th>Duration (days)</th>
<th>Blindness</th>
<th>Diagnosis</th>
<th>Exclusions</th>
<th>Data Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>2N = 5</td>
<td>Active control with</td>
<td>- Watched a music video sing-a-long for 20 mins and then received a snack</td>
<td>older individual with cognitive impairment who were to be discharged to their homes or residential home</td>
<td>Mean 35</td>
<td>Age: Mean 80</td>
<td>young people, MMSE &lt;10 &gt;24, Cambridge Cognitive Screening Test &gt;78/80, cognitive impairment and depression/moderate psychiatric disorder, should be admitted to a nursing home, absence of occupational therapy recommendations and reviewed with the caregiver during a home visit. Follow-up and assessment 1-6 months later.</td>
</tr>
<tr>
<td>Study Type</td>
<td>Data Used</td>
<td>Group 1 N= 186</td>
<td>Group 2 N= 192</td>
<td></td>
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<td>--------------------</td>
<td>---------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>JENSEN2003</td>
<td>n= 378</td>
<td>Combined intervention with - Participated in intervention program for 11 weeks, which targeted general and resident-specific risk factors for falling. Program inc. staff education, environmental modification, exercise, supply and repair of aids, change in medication, hip protectors.</td>
<td>No treatment with - Control group</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Study Type: RCT (cluster)</td>
<td>Age: Mean 83  Sex: 234 males 144 females  Diagnosis: 20% Unspecified dementia  Exclusions: No info  Baseline: MMSE: High level of cognition group = 13, low level of cognition group = 24</td>
<td></td>
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<tr>
<td>Study Description: Preplanned subgroup comparison of the effectiveness of a cluster-randomised, nonblinded, usual care, controlled trial.</td>
<td></td>
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</tr>
<tr>
<td>Blindness: Open</td>
<td>Data Used Number of falls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 77</td>
<td>Setting: Nine residential facilities in Sweden</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Setting: Nine residential facilities in Sweden</td>
<td>Info on Screening Process: 439 screened 61 excluded No consent, in hospital, died.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JOSEPHSSON1995</td>
<td>n= 4</td>
<td>Occupational therapy with - Individual program designed for each p based upon one chosen activity and designed to make it less dependent on higher-order cog func's and more on procedural motor skills, through, environmetal adaptation and adjusting therapists approach.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type: Non-comparative study</td>
<td>Age: Mean 79  Range 70-85  Sex: 1 male 3 females  Diagnosis: 75% Alzheimer’s disease by DSM III-R  Exclusions: No info  Baseline: MMSE's of 7, 20, 9 and 14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Description: 4 subjects followed intervention program and were pretested and posttested on their ability to complete ADL</td>
<td>Data Used Assessment of Motor and Process Skills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blindness: Open</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Setting: Psychogeriatric day care centre where they resided in Stockholm, Sweden.</td>
<td>Info on Screening Process: No info</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KELLY2002</td>
<td>n= 47</td>
<td>Technological device with - Creditcard size device with adhesive patch, worn on thigh. Wireless, disposable, water &amp; shock proof and unobtrusive. When a patient's leg becomes weight bearing, the receiver emits an audible signal which both alerts the patient to sit and summons carer.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type: Before-After study/ Interrupted time series</td>
<td>Data Used Number of falls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Description: Crossover design. Patient wore device for one week and were monitored for fall activity before, during and after this week.</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Blindness: Open</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 7</td>
<td>Followup: 10 days</td>
<td></td>
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</tr>
<tr>
<td>Followup: 10 days</td>
<td>Setting: Medicare unit of a skilled nursing facility in northern California</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Setting: Medicare unit of a skilled nursing facility in northern California</td>
<td>Info on Screening Process: No info</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCMURDO1995</td>
<td>n= 69</td>
<td>Active control with - Health education program: visited at home for 30 mins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type: RCT (individual)</td>
<td>Age: Mean 82  Range 75-96  Sex: 61 males 6 females  Diagnosis: Fall Risk Assessment &gt;6 (mild to moderate risk), Nonambulatory.  Notes: At least 50% were described as demented by the medical record, although formal mental status testing was not part of the study design.  Baseline: None</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Study Description:</td>
<td>Data Used ADL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Description:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blindness: Open</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration (days):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Followup:</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Group 1 N= 26</td>
<td>Exercise with - 5 days a week for maximum of 8 weeks. Strength exercises (3 times/week) consisted of resistance training of both knees, shoulders, elbows, and ankles. Endurance training (2 times/week) using either upper extremity ergometer, a stationary cycle, stepper.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group 2 N= 32</td>
<td>Standard Care with</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MEULEMANN2000**

**Study Type:** RCT (individual)

**Blindness:** Single blind

**Duration (days):** Mean 70

**Followup:** 12 months

**Setting:** Participants recruited from Veterans Association nursing home, Geriatric Evaluation and Management unit, and Community Nursing Home in the US

**Info on Screening Process:** 81 gave informed consent, 3 dropped out during testing, 20 dropped out after testing but before they could be retested 4-8 weeks later (10 because they were discharged home, 5 because they became ill, 4 died)

**n= 58**

**Age:** Mean 75

**Sex:** 53 males 5 females

**Diagnosis:**

Exclusions: <60 years old, no Physical Activities of Daily Living needed for help, expected length of stay <4 weeks, uncontrolled hypertension, unstable angina pectoris, other medical conditions that would interfere with safety of training protocol, could not follow simple instructions (i.e. severely demented), subjects in wheelchairs needing more than moderate assistance to transfer, had a stroke in previous 3 weeks, had a pacemaker or chronic atrial fibrillation

**Baseline:** MMSE = 23

**Data Used:**

<table>
<thead>
<tr>
<th>PADL</th>
<th>IADL</th>
</tr>
</thead>
</table>

**Results from this paper:**

**Internal Validity:***

1.1 Well covered
1.2 Well covered
1.3 Adequately addressed
1.4 Adequately addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Well covered
1.8 Strength group = 23.8% drop out, Mobility group = 50% drop out, Health Education (Active control) = 7.1% drop out
1.9 Not addressed
1.10 Not applicable

**Overall Assessment of the Study:**

2.1 1+
2.2 favours treatment
2.3 yes
2.4 MCI (MMSE =25)
<table>
<thead>
<tr>
<th><strong>MIHAELIDIS2001</strong></th>
<th><strong>Data Used</strong></th>
<th><strong>Group N= 1</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Type:</strong> Non-comparative study</td>
<td>Independently completing task</td>
<td>Technological device with Device provided reminders of the sequence of steps involved in handwashing only. It prompted him to enter the washroom and assist when necessary. Gave cues, such as, turn water on, pick up soap, rinse off all soap.</td>
</tr>
<tr>
<td><strong>Study Description:</strong> Single-subject pilot study to test the device.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blindness:</strong> Open</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration (days):</strong> Mean 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Setting:</strong> Conducted in the washroom of an unoccupied patient room located on the Cognitive Support Unit of a Canadian hospital.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Info on Screening Process:</strong> 5 screened 4 excluded Independent during handwashing activities, broken hip, suffered cerebral vascular accident.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MORRIS1999</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study Type:</strong> RCT (cluster)</td>
<td></td>
<td>51% participants with dementia should it be included?</td>
</tr>
<tr>
<td><strong>Study Description:</strong> controlled for baseline differences through multivariate weighting - included functional status, cognitive status, age</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blindness:</strong> Single blind</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration (days):</strong> Mean 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Setting:</strong> 6 nursing homes in the US with 80 or more long stay nursing home beds</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Info on Screening Process:</strong> 849 screened, 349 excluded (100 died, 55 too sick, 162 refused to participate, 32 family unavailable, 32 didn’t meet inclusion criteria)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NOWALK2001</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study Type:</strong> RCT (individual)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blindness:</strong> Single blind</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration (days):</strong> Mean 730</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Setting:</strong> 2 senior housing communities in the US each with a variety of living arrangements ranging from independent living to skilled nursing care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1 N= 36</td>
<td>Group 2 N= 38</td>
<td>Group 3 N= 35</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Exercise with - Prompted voiding and exercise. The exercise was integrated into the PV incontinence care routine. Emphasis on exercises specific to the functional skills required for toileting and other ADLs - sit-to-stands, propelling wheelchairs or walking.</td>
<td>Exercise with - 2 components: 1) living and learning (once a month): designed to reduce fear of falling through behavioural and psychotherapeutic methods 2) tai-chi (3 times/week): to improve factors affecting balance and body awareness</td>
<td>Active control with - comprehensive, collaborative falls prevention program that included team management and 3 educational programs to enhance quality of life</td>
</tr>
</tbody>
</table>

Info on Screening Process: 361 screened: 69 had catheters, 20 did not pass cognitive screening, 173 did not respond to prompted voiding, 5 irreversible physical limitations, 26 did not complete treatment

Baseline: MMSE = 11.6

<table>
<thead>
<tr>
<th>SCHNELLE1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Type: RCT (individual)</td>
</tr>
<tr>
<td>Study Description: 4-6 week phase to test responsiveness to prompted voiding before randomization</td>
</tr>
<tr>
<td>Blindness: Open</td>
</tr>
<tr>
<td>Duration (days): Mean 56</td>
</tr>
<tr>
<td>Setting: residents from 4 nursing homes in US</td>
</tr>
</tbody>
</table>

Data Used
- Number of stands
- Walking endurance

Results from this paper:
- Internal Validity:
  - 1.1 Well covered
  - 1.2 Not reported
  - 1.3 Not addressed
  - 1.4 Adequately addressed
  - 1.5 Adequately addressed
  - 1.6 Adequately addressed
  - 1.7 Well covered
  - 1.8 27.3% dropped out
  - 1.9 Well covered
  - 1.10 Not reported

Overall Assessment of the Study:
- 2.1 1+
- 2.2 favours treatment
- 2.3 yes
- 2.4 participants with MMSE = 25

<table>
<thead>
<tr>
<th>SCHNELLE1995</th>
<th>SCHNELLE1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Used</td>
<td>Data Used</td>
</tr>
<tr>
<td>Number of stands</td>
<td>Number of stands</td>
</tr>
<tr>
<td>Walking endurance</td>
<td>Walking endurance</td>
</tr>
</tbody>
</table>

Baseline: MMSE = 25, IADL = 10
**Overall Assessment of the Study:**

- 2.1 1+
- 2.2 favours treatment
- 2.3 yes
- 2.4 yes

### SCHNELLE1996

**Study Type:** RCT (individual)

- Blinding: Single blind
- Duration (days): Mean 224

Setting: Residents from 3 proprietary nursing homes and 1 non-profit nursing home in US

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1 N= 94</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>Exercise with</td>
</tr>
<tr>
<td></td>
<td>- Four care episodes a day, 5 days a week. During each part of intervention received prompted voiding. Before or after incontinence care staff encouraged residents to walk/wheel their chairs, and to repeat sit-to-stands. Once a day upper body training.</td>
</tr>
<tr>
<td>Number of stands</td>
<td></td>
</tr>
</tbody>
</table>

### SCHNELLE2002

**Study Type:** RCT (individual)

- Blinding: Single blind
- Duration (days): Mean 224

Setting: Residents from 3 proprietary nursing homes and 1 non-profit nursing home in US

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1 N= 94</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>Exercise with</td>
</tr>
<tr>
<td></td>
<td>- Four care episodes a day, 5 days a week. During each part of intervention received prompted voiding. Before or after incontinence care staff encouraged residents to walk/wheel their chairs, and to repeat sit-to-stands. Once a day upper body training.</td>
</tr>
<tr>
<td>Number of stands</td>
<td></td>
</tr>
</tbody>
</table>

### SHAW2003A

**Study Type:** RCT (individual)

**Study Description:** Prospective single centre randomised control trial of multifactorial assessment and intervention after a fall.

- Blinding: Single blind
- Duration (days): 1 yr

Setting: Two A&E departments, Newcastle-Upon-Tyne

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1 N= 130</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>Combined intervention with</td>
</tr>
<tr>
<td></td>
<td>- Multifactorial intervention including treating medical problems, cardiovascular advice, feet, footwear, gait and balance, environmental fall hazards.</td>
</tr>
<tr>
<td>Number of falls</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 2 N= 144</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>No treatment with</td>
</tr>
<tr>
<td></td>
<td>- Conventional care only</td>
</tr>
<tr>
<td>Number of falls</td>
<td></td>
</tr>
</tbody>
</table>
### SHIMADA2003

**Study Type:** RCT (individual)  
**Study Description:** Randomised three-group parallel group study. Non-blind because the authors themselves performed both examination and intervention.  
**Blindness:** Open  
**Duration (days):** Mean 84  
**Setting:** Geriatric health services facility in Japan, 21 community dwelling, 13 institutionalised  
**Info on Screening Process:** 81 screened 47 excluded  
Severe impairment, dementia, did not agree to participate  

<table>
<thead>
<tr>
<th>Group</th>
<th>Data Used</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Balance exercise</td>
<td>40 minutes, 2-3 times weekly, for 12 weeks</td>
</tr>
<tr>
<td>2</td>
<td>Gait exercise</td>
<td>40 minutes, 2-3 times weekly, for 12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>No treatment</td>
<td></td>
</tr>
</tbody>
</table>

**Diagnosis:**  
Age: Mean 81  
Sex: 5 males 29 females  
Exclusions: Severe impairment, dementia, did not agree to participate  
Baseline: Hasegawa's dementia scale: Control = 16.7, Balance exercise, 21.2, Gait exercise = 17.0

### TAPPEN1994

**Study Type:** RCT (individual)  
**Study Description:** 3 group, pretest-posttest, experimental design. No info on how they were randomised.  
**Blindness:** Single blind  
**Duration (days):** Mean 140  
**Setting:** Nursing homes, US  
**Info on Screening Process:** No info as randomly selected from population of 240  
Severe impairment, dementia, did not agree to participate  

<table>
<thead>
<tr>
<th>Group</th>
<th>Data Used</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Exercise with</td>
<td>Functional skill training - focus on regaining function in basic activities of daily living through repeated practice of each. Verbal prompting, physical demonstration and positive reinforcement were used. 5 days/wk, 2.5 hrs a day, 20 wks</td>
</tr>
<tr>
<td>2</td>
<td>Active control with</td>
<td>Stimulation - adult games, group discussion about pastimes and interests, music, simple relaxation, such as deep breathing and light massage. 5 days/wk, 2.5 hrs a day, 20 wks</td>
</tr>
<tr>
<td>3</td>
<td>Standard Care with</td>
<td>Regular nursing care</td>
</tr>
</tbody>
</table>

**Diagnosis:**  
Age: Mean 84 Range 59-102  
Sex: 16 males 47 females  
Exclusions: No chart diagnosis of dementia, <6 errors on the Short Portable Mental Status Questionnaire, inability to stand with assistance. Evidence of stroke, head injury, major psychiatric problem or mental retardation.  
Baseline: Performance test of ADL: Skill training = 43.01, Stimulation = 43.45, Control = 42.62

### TAPPEN2000

**Study Type:** RCT (individual)  
**Blindness:** Single blind  
**Duration (days):**  
**Setting:** Inpatient units of 2 long term care facilities both in Florida  
Severe impairment, dementia, did not agree to participate  

<table>
<thead>
<tr>
<th>Group</th>
<th>Data Used</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Exercise with</td>
<td>30 minutes, 3 days a week for, of self-paced assisted walking interspersed with rest as needed to delay fatigue</td>
</tr>
<tr>
<td>2</td>
<td>Conversation with</td>
<td>Group discussion about pastimes and interests, music, simple relaxation, such as deep breathing and light massage. 5 days/wk, 2.5 hrs a day, 20 wks</td>
</tr>
<tr>
<td>3</td>
<td>Exercise + Conversation with</td>
<td>Walking exercise and conversation treatment 3 times a week for 16 weeks</td>
</tr>
</tbody>
</table>

**Diagnosis:**  
Age: Mean 89  
Sex: no information  
Exclusions: Not able to stand and walk with assistance of one individual and/or an assistive device, do not have physician clearance to participate in walking exercise, evidence of vascular dementia, stroke, PD, history of major depression, schizophrenia, mental retardation  
Baseline: MMSE = 10.5

### Results from this paper:  
4798 excluded  
MMSE score, medical reasons, residence problems, communication difficulties, death, inability to walk.  
**Site, had no major informant.**  
Baseline: MMSE: Intervention group = 14, control group = 12  

**Data Used**  
- Performance Orientated Mobility Assessment  
- Functional Balance Scale  
- Manual Perturbation Test  
- Functional Reach Test  
- One Leg Standing Test  
- Stair Climbing/Descending Test  
- Timed 'Up and Go' Test
### Internal Validity:
- 1.1 Adequately addressed  
- 1.2 Not reported  
- 1.3 Not addressed  
- 1.4 Adequately addressed  
- 1.5 Adequately addressed  
- 1.6 Adequately addressed  
- 1.7 Adequately addressed  
- 1.8 8.5% drop out  
- 1.9 Not addressed  
- 1.10 Not addressed

**Overall Assessment of the Study:**
- 2.1 1+  
- 2.2 favours treatment  
- 2.3 yes  
- 2.4 yes

### Data Used
- **TERI2003**
  - **Study Type:** RCT (individual)  
  - **Study Description:** Carer and patient dyads  
  - **Type of Analysis:** Intention to treat  
  - **Follow-up:** 5 years  
  - **Setting:** Community based people with AD in the US  
  - **Info on Screening Process:** 381 screened, 228 excluded (144 not eligible, 74 refused participation, 10 not able to be contacted)  
  - **n = 153**  
  - **Age:** Mean 78  
  - **Sex:** 90 males  
  - **Diagnosis:** 100% Alzheimer's disease by NINCDS-ADRDA  
  - **Exclusions:** not community dwelling, non-ambulatory, carer not willing to participate  
  - **Baseline:** MMSE = 17

- **TOULOTTE2003**
  - **Study Type:** RCT (individual)  
  - **Blindness:** Single blind  
  - **Duration (days):** Mean 117  
  - **Setting:** Dementia patients with a history of falling  
  - **n = 20**  
  - **Age:** Mean 81  
  - **Sex:** no information  
  - **Diagnosis:**  
  - **Exclusions:** <2 falls at home or in an institution, couldn't

### Notes:
- **subscales of SF-36 and SIP used**
- **Exercise + Behavioural Intervention**  
  - **Followup:** 5 years  
  - **Setting:** Community based people with AD in the US  
  - **Duration (days):** Mean 117  
  - **Blindness:** Single blind  
  - **Study Type:** RCT (individual)  
  - **N = 10**  
  - **Exercise with - 2 supervised 1h exercise sessions per week for 16 weeks. At each session subjects undertook exercises to develop muscular strength, proprioception, static and dynamic balance and flexibility.**
### Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Setting</th>
<th>Duration (days)</th>
<th>Blindness</th>
<th>Study Type</th>
<th>Info on Screening Process</th>
<th>Baseline</th>
<th>Data Used</th>
<th>Group</th>
<th>N</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT (individual)</td>
<td>Community dwelling frail older people, Denmark</td>
<td>Mean 84</td>
<td>Single blind</td>
<td>RCT (individual)</td>
<td>103 fulfilled criteria, 57 excluded (41 did not wish to participate, 7 functional ability too good, withdrew due to serious illness, 2 died); after randomization 2 excluded (1 died, 1 serious illness)</td>
<td>MMSE = 24</td>
<td>SF-36, Berg's Balance Scale</td>
<td>2</td>
<td>22</td>
<td>Not RCT</td>
</tr>
</tbody>
</table>

### Results from this paper:

**Internal Validity:**
1. Well covered
2. Not reported
3. Not addressed
4. Adequately addressed
5. Adequately addressed
6. Adequately addressed
7. Adequately addressed
8. Not reported
9. Not addressed
10. Not applicable

**Overall Assessment of the Study:**
2.1 1+
2.2 favours treatment
2.3 yes
2.4 mildly impaired participants

### Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAKKER2001</td>
<td>Not RCT</td>
</tr>
</tbody>
</table>
BAKKER2004  Not actually looking at promoting independence
BALLARD2001  No intervention
BROWN1998  Non-dementia participants
CLEMSON1996
FRIEDMAN1991  Not dealing with promoting independence directly
GOTESTAM1990  Not required intervention
HAGEMAN2002  Non RCT
HEYN2003  Not promoting independence
MACRAE1996  Non RCT
MCGLITON2003  Not required intervention
MCMURDO1993  No information provided about cognitive impairment or dementia
MCMURDO1994  Can't locate paper
SHAW2002  Review
STAMFORD1974  Can't locate paper
VANSCHOOR2003  Non-dementia participants
VERDOTEROBERTSO2000  Non RCT

References of Included Studies

BUETTNER1997  (Published Data Only)

CHANDLER1998  (Published Data Only)

COTT2002  (Published Data Only)

DOOLEY2004  (Published Data Only)

FRANCESE1997  (Published Data Only)

GRAFF2003  (Published Data Only)

JENSEN2003  (Published Data Only)

JOSEPHSSON1995  (Published Data Only)

KELLY2002  (Published Data Only)
MCURDO1995 (Published Data Only)

MEULEMAN2000 (Published Data Only)

MIHAIDIS2001 (Published Data Only)

MORRIS1999 (Published Data Only)

NOWALK2001 (Published Data Only)

SCHNELLE1995 (Published Data Only)

SCHNELLE1996 (Published Data Only)

SCHNELLE2002 (Published Data Only)

SHAW2003A (Published Data Only)

SHIMADA2003 (Published Data Only)

TAPPEN1994 (Published Data Only)

TAPPEN2000 (Published Data Only)

TERI2003 (Published Data Only)

TOULLET2003 (Published Data Only)

WORM2001 (Published Data Only)

References of Excluded Studies

BAKKER2001 (Published Data Only)
BAKKER2004 (Published Data Only)

BALLARD20001 (Published Data Only)

BROWN1998 (Published Data Only)

CLEMSON1996 (Published Data Only)

FRIEDMAN1991 (Published Data Only)

GOTESTAM1990 (Published Data Only)

HAGEMAN2002 (Published Data Only)

HEY2003 (Published Data Only)

MACRAE1996 (Published Data Only)

MCGILTON2003 (Published Data Only)

MCMURDO1993 (Published Data Only)

MCMURDO1994 (Published Data Only)

SHAW2002 (Published Data Only)

STAMFORD1974 (Published Data Only)

VANSCOTHEROBERTSO2000 (Published Data Only)

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Table 4: Included/excluded studies table for review of psychosocial interventions for the treatment of cognitive symptoms of dementia

<table>
<thead>
<tr>
<th>Characteristics of Included Studies</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BAINES1987</strong></td>
<td>n=15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type: RCT (individual)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Description: Cross-over trial + no treatment group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blindness: No mention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Setting: Residents of a large local authority home in UK with moderate/severe impairment of cognitive function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Info on Screening Process: 20 screened: 3 excluded because of communication problems, 2 excluded because they didn't have cognitive impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusions: Severe communication problems, &lt;moderate cognitive impairment (according to Information/Orientation and Mental ability scores of the CAPE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline: Group A: information/orientation = 5.4, mental ability = 6.8; Group B: information/orientation = 5.8, mental ability = 6.2; Group C (control): information/orientation = 5.9, mental ability = 7.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data Used</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behaviour Rating Scale (CAPE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental ability (CAS)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Information/orientation (CAS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group 1 N=5</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Reality Orientation with - Group met for 30 mins/day Monday-Friday for 4 weeks. Used a large board for recording day, month, weather, writing materials, old newspapers etc. Also used materials to stimulate all 5 senses (e.g. distinctive smells, vials of rose water)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reminiscence Therapy with - Group met for 30 mins/day Monday-Friday for 4 weeks. Set of 6 audio/slide programmes used to facilitate reminiscence from Help the Aged, old photographs of local scenes, residents' personal photos, books, magazines, newspapers</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Group 2 N=5</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation therapy with - Group met for 30 mins/day Monday-Friday for 4 weeks. Set of 6 audio/slide programmes used to facilitate reminiscence from Help the Aged, old photographs of local scenes, residents' personal photos, books, magazines, newspapers</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Comparisons Included in this Clinical Question</strong></th>
<th><strong>Included/excluded studies</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive rehabilitation vs active control</td>
<td>LOEWENSTEIN2004</td>
</tr>
<tr>
<td>Computerised memory training vs social support</td>
<td>HEISS1994</td>
</tr>
<tr>
<td>Memory training vs active control</td>
<td>CAHNWEINER2000 DAVIS2001</td>
</tr>
<tr>
<td>Memory training vs social support</td>
<td>QUAYHAGEN2000</td>
</tr>
<tr>
<td>Memory training vs waitlist control</td>
<td>CORBEIL1999 KOLTAI2001 QUAYHAGEN2000</td>
</tr>
<tr>
<td>Snoezelen (multi-sensory stimulation) vs active control</td>
<td>BAKER2003</td>
</tr>
<tr>
<td>Validation therapy vs social contact</td>
<td>ROBB1986 TOSELAND1997</td>
</tr>
<tr>
<td>Validation therapy vs standard care</td>
<td>TOSELAND1997</td>
</tr>
<tr>
<td>Study Type: RCT (individual)</td>
<td>No treatment with</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Type of Analysis: Intention to treat</td>
<td></td>
</tr>
<tr>
<td>Blindness: Open</td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 30</td>
<td></td>
</tr>
<tr>
<td>Followup: One month after sessions</td>
<td></td>
</tr>
<tr>
<td>Setting: Multi-centre trial: UK (patients of a day hospital), Netherlands (residents of a psychogeriatric ward), Sweden (residents of a psychogeriatric ward)</td>
<td></td>
</tr>
<tr>
<td>Info on Screening Process: 20 participants from Netherlands sample excluded before randomization: 8 transferred to another ward, 5 died, 3 not given informed consent, 4 carers did not respond to original letter</td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**

**BAKER2003**

<table>
<thead>
<tr>
<th>Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 N= 55</td>
<td></td>
</tr>
<tr>
<td>Multi-sensory stimulation with - 8 standardized sessions (duration of 30 minutes), for 4 weeks, twice a week. Non-directive and enabling, special effects to stimulate all senses except taste, unpatterned non-sequential stimuli, no intellectual demands</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2 N= 62</td>
<td></td>
</tr>
<tr>
<td>Active control with - 8 standardized sessions (duration of 30 minutes), over 4 weeks, twice a week. Directive, no intended special multi-sensory experience, patterned often sequential stimuli, intellectual/physical demands specific to the task.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>REHAB</td>
<td></td>
</tr>
<tr>
<td>Behaviour and Mood Disturbance Scale</td>
<td></td>
</tr>
<tr>
<td>Behaviour Rating Scale (CAPE)</td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CERAD: neuropsychological tests</td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
</tr>
</tbody>
</table>

**BREUIL1994**

<table>
<thead>
<tr>
<th>Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 N= 56</td>
<td></td>
</tr>
<tr>
<td>Cognitive Stimulation with - 10 sessions, of 1 hour, over 5 weeks e.g. shown dotted outline of umbrella and asked to join dots. Then asked to draw umbrella closed and upside down to evoke associated words (e.g. rain, raincoat, boots), to talk about rainy months and regions of France</td>
<td></td>
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<table>
<thead>
<tr>
<th>Group</th>
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<tbody>
<tr>
<td>2 N= 50</td>
<td></td>
</tr>
<tr>
<td>No treatment with</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
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<tbody>
<tr>
<td>MMSE</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CERAD tests: 4 items not used because of ceiling effects (e.g. naming procedure, constructional praxis, word list recognition); 1 item (word list recall) not used because of floor effects - only 2 items used (word list, verbal fluency)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
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<tr>
<th>Data Used</th>
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<tbody>
<tr>
<td>MMSE</td>
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<table>
<thead>
<tr>
<th>Diagnosis:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s disease</td>
<td></td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td></td>
</tr>
<tr>
<td>Mixed Dementia</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusions:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>no informed consent from consultant psychiatrist or family members; no diagnosis of Alzheimer’s, vascular or mixed dementia; major psychiatric co-morbidities; confined to bed; MMSE &gt;17;</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>n= 117</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Age: Mean 82</td>
<td></td>
</tr>
<tr>
<td>Sex: no information</td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td></td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td></td>
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<tr>
<td>Mixed Dementia</td>
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<tr>
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<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>n= 56</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age: Mean 77</td>
<td></td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
</tr>
<tr>
<td>100% Unspecified dementia by DSM III</td>
<td></td>
</tr>
<tr>
<td>Alzheimer’s disease by CERAD</td>
<td></td>
</tr>
<tr>
<td>Multi-infarct dementia by CERAD</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusions:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>no informed consent from consultant psychiatrist or family members; no diagnosis of Alzheimer’s, vascular or mixed dementia; major psychiatric co-morbidities; confined to bed; MMSE &gt;17;</td>
<td></td>
</tr>
</tbody>
</table>
Exclusions: CERAD exclusion criteria: MMSE > 9; impaired hearing and vision severe enough to interfere with tests; severe aphasia; behavioral disorder incompatible with integration within a group for an hour; dementia due to potentially treatable causes

5 excluded because they did not attend all evaluation and training sessions

Results from this paper:
Internal validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Not addressed
1.4 Adequately addressed
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Adequately addressed
1.8 Cognitive stimulation = 9% drop out; control group = 7% drop out
1.9 Not addressed
1.10 Not applicable

Overall Assessment of the study:
2.1 1+
2.2 Favours treatment
2.3 Yes
2.4 Yes

CAHNWEINER2003

Study Type: RCT (individual)

Blinding: Single blind
Duration (days): Mean 42
Followup: 8 weeks

Info on Screening Process: 5 withdrew due to transportation problems getting to the clinic

n = 34
Age: Mean 78
Sex: 20 males 14 females

Diagnosis:
100% Alzheimer's disease by NINCDS-ADRDA

Baseline: MMSE: Memory training group = 24.3, Control group = 25.1

Group 1 N = 17
Memory Training with - 6 sessions over a period of 6 weeks based on the ACTIVE study (Jobe et al 2001). Includes instruction and extensive practice in multiple mnemonic strategies (e.g. organizing stimulus items into meaningful categories, organizing ideas and details)

Group 2 N = 17
Active control with - A weekly 45 minute group in which educational information about aging and dementia was presented. Topics included: overview of memory; changes in cognitive function with normal aging; dementia/AD overview; depression, anxiety, and sleep disturbance

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Not addressed
1.4 Adequately addressed
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Adequately addressed
1.8 Not reported
## CORBEIL1999

**Study Type:** RCT (individual)  
**Blindness:** Single blind  
**Duration (days):** Mean 84  
**Followup:** 9 months  
**Setting:** Community dwelling people with dementia and carer dyads in the US  
**Notes:** Some assessors were not blinded  
**Info on Screening Process:** No screened = 132 people with dementia and carer dyads  
No. excluded = 37 excluded because they didn't meet inclusion criteria, 8 excluded because they did not provide complete data up to follow up

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory Training with</td>
<td>- 6 days a week, for 1 hour, over 12 weeks. Carers were trained each week in activities to stimulate their partner in areas of memory, problem solving, and conversational fluency.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo with</td>
<td>- 6 days a week for 1 hour over 12 weeks. Followed same time frames and had the same exposure to the researchers as did the experimental condition. Only difference was that the activities were passive e.g watching TV without encouraging active involvement.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waitlist with</td>
<td>- On waitlist for 9 months then offered treatment. Due to continued deterioration only 5 dyads opted for complementary sessions</td>
</tr>
</tbody>
</table>

### Data Used
- Dementia Rating Scale  
- Notes: All other outcomes composites of scales - validity of composites not investigated

### Results from this paper:

**Internal Validity:**  
1.1 Adequately addressed  
1.2 Adequately addressed  
1.3 Not reported  
1.4 Poorly addressed  
1.5 Adequately addressed  
1.6 Poorly addressed  
1.7 Adequately addressed  
1.8 8% dropped out of whole sample  
1.9 Not addressed  
1.10 Not applicable

### Overall Assessment of the Study:
- 2.1 1+  
- 2.2 in favour of placebo or treatment  
- 2.3 no  
- 2.4 yes

## DAVIS2001

**Study Type:** RCT (individual)  
**Study Description:** placebo group crossed over after 5 weeks of treatment to the intervention for a further 5 weeks  
**Blindness:** Single blind  
**Duration (days):** Mean 70  
**Setting:** Alzheimer's disease research centre at Baylor College of Medicine, Texas USA

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive training with</td>
<td>- 1 hour sessions (individually), weekly, for 5 weeks. Began testing patient's recall of personal info, followed by spaced retrieval (not for those answered all correct), peg task, face-name training task. Also cognitive stimulation- 30 mins, 6 days/week</td>
</tr>
</tbody>
</table>

### Data Used
- Wechsler Adult Intelligence Scale-Digit Span  
- WMS-R Visual Reproduction  
- WMS-R Logical Memory  
- MMSE

### Results from this paper:

**Internal Validity:**  
1.1 Adequately addressed  
1.2 Adequately addressed  
1.3 Not reported  
1.4 Poorly addressed  
1.5 Adequately addressed  
1.6 Poorly addressed  
1.7 Adequately addressed  
1.8 Adequately addressed  
1.9 Not addressed  
1.10 Not applicable

### Overall Assessment of the Study:
- 2.1 1+  
- 2.2 in favour of placebo or treatment  
- 2.3 no  
- 2.4 yes
Baseline: MMSE: placebo group = 22.78, intervention group = 21.84; GDS: placebo group = 5.67, intervention group = 4.37

Group 1 N= 18
Placebo with - Individual weekly 1 hour sessions for 5 weeks. Unstructured conversation and questioning by the examiner. Asked how memory was doing and had patients recite overlearned material (e.g. alphabet, months of year). Also watched health videos.
Cognitive training with - after active control of 5 weeks crossed over to receive cognitive training

Results from this paper:
Internal Validity: 1.1 Adequately covered 1.2 Adequately addressed 1.3 Not addressed 1.4 Adequately addressed 1.5 Adequately addressed 1.6 Poorly addressed 1.7 Well covered 1.8 Intervention group = 0 drop out, Placebo group =22% 1.9 Not addressed 1.10 Not applicable
Overall Assessment of the Study: 2.1 1+ 2.2 Favoured treatment 2.3 not certain 2.4 yes

FERRARO1991
Study Type: RCT (individual)
Blindness: No mention
Duration (days): Mean 168
Setting: Italy: institutionalized patients
Notes: Randomization not mentioned in paper but when contacted by Spector et al (2000) indicated it was randomized but gave no details of the method

n= 19
Age: Mean 83
Sex: 11 males  8 females
Diagnosis:
100% Unspecified dementia by MMSE
Exclusions: exclusions: use of pharmacological therapies for cognitive function, anaemias, those with severe metabolic and/or cardiorespiratory failure, noisy or violent, severely incontinent, bedridden, marked visual or hearing impairment, MMSE not between 18-25
Treatment group: mean for CAS: information/orientation = 8.15, mental ability = 7.69, psychomotor performance = 7.69, total score = 23.54; mean MOSES: self care functioning = 19.15, disoriented behavior = 12.46, depressed anxious mood = 14.69, irritable behavior = 9.38, withdrawn behavior = 17.77

Group 1 N= 13
Reality Orientation with - 1 hour formal session, 5 times a week, for 24 weeks. There was a 3 week break for Christmas and Easter holidays
Group 2 N= 6
No treatment with

Results from this paper:
Internal Validity: 1.1 Adequately addressed
### GOLDWASSER1987

**Study Type:** RCT (individual)

- **Blindness:** Single blind
- **Duration (days):** Mean 35
- **Setting:** Beth Sholom Home, Virginia, US
- **Info on Screening Process:** 1 died in reminiscence group during trial, 1 subject from both control groups dropped from analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Reminiscence Therapy with - 30 mins reminiscence groups twice a week for 5 weeks.</td>
</tr>
<tr>
<td>2.</td>
<td>Social contact with - Support group focused on present or future events and problems. This group met for 30 mins twice weekly for 5 weeks.</td>
</tr>
<tr>
<td>3.</td>
<td>No treatment with</td>
</tr>
</tbody>
</table>

**Data Used**
- BDI
- MMSE
- ADL

**Baseline:** MMSE = 10.4

**Results from this paper:**

- **Internal Validity:**
  1.1 Adequately addressed
  1.2 Not reported
  1.3 Not addressed
  1.4 Adequately addressed
  1.5 Adequately addressed
  1.6 Adequately addressed
  1.7 Well covered
  1.8 3.7% drop out
  1.9 Not addressed
  1.10 Not applicable

**Overall Assessment of the Study:**
- 2.1 1+
- 2.2 either direction
- 2.3 no
- 2.4 applicable but does not distinguish between types of dementia

**Conclusions:** For cognition there were no significant main effects for cognition. For affect there was no significant main effects for treatment, but significant main effects for period F(2,24) = 7.27, p<0.01 indicating BDI scores changed over time. For behaviour there were no significant effects.

### HEISS1994

**Study Type:** RCT (individual)

- **Blindness:** Open
- **Duration (days):** Mean 180

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Support with - 1 hour each week for 6 months. Participants spoke about their personal problems and how they managed their daily lives. Sometimes</td>
</tr>
</tbody>
</table>

**Data Used**
- MMSE
- Golin's incomplete picture task
- Corsi's tapping task

**n= 70**
- Age: Range 48-79
- Sex: 37 males  33 females

**Results from this paper:**

- **Internal Validity:**
  1.1 Adequately addressed
  1.2 Not reported
  1.3 Not addressed
  1.4 Adequately addressed
  1.5 Adequately addressed
  1.6 Adequately addressed
  1.7 Well covered
  1.8 3.7% drop out
  1.9 Not addressed
  1.10 Not applicable

**Overall Assessment of the Study:**
- 2.1 1+
- 2.2 favours treatment
- 2.3 no
- 2.4 yes
<table>
<thead>
<tr>
<th>Group 1</th>
<th>N=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory Training with - 8 received individual memory training and 8 received group memory training. For group memory training participants received 5 1 hour weekly sessions. Individual memory training group received 6 one-on-one sessions.</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>N=8</td>
</tr>
<tr>
<td>Waitlist with</td>
<td></td>
</tr>
</tbody>
</table>

**KOLTAI2001**

| Study Type: RCT (individual)  |
|---|---|
| Blindness: No mention  |
| Duration (days): Mean 35  |
| Followup: 47 days  |
| Setting: Referred to the study from Bryan ADRC Neurological Disorders Clinic, US. All participants had mild to moderate dementia  |

| n=22  |
|---|---|
| Age: Mean 73  |
| Sex: no information  |

**Data Used**

CERAD: neuropsychological tests

<table>
<thead>
<tr>
<th>Group</th>
<th>N=18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive rehabilitation with - For 1 hour twice a week for 6 months. Participants had to solve different memory, perceptual, or motor tasks.</td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>N=17</td>
</tr>
<tr>
<td>Cognitive rehabilitation with - For 1 hour twice a week for 6 months. Participants had to solve different memory, perceptual, or motor tasks.</td>
<td></td>
</tr>
<tr>
<td>Pyritinol with . Mean dose 600mg - Oral Pyritinal 600mg twice daily</td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>N=18</td>
</tr>
<tr>
<td>Cognitive rehabilitation with - For 1 hour twice a week for 6 months. Participants had to solve different memory, perceptual, or motor tasks.</td>
<td></td>
</tr>
<tr>
<td>Phosphatidylserine with . Mean dose 200mg - Oral phosphatidylserine 200 mg twice daily</td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**

**Internal Validity:**

1.1 Well covered
1.2 Adequately covered
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Adequately covered
1.7 Adequately addressed
1.8 12.5% drop out for whole sample
1.9 Not addressed
1.10 Not applicable

**Overall Assessment of the Study:**

2.1 1+
2.2 Favours treatment
2.3 yes
2.4 yes
Results from this paper:
Internal Validity:
1.1 Adequately addressed
1.2 Adequately addressed
1.3 Not reported
1.4 Well covered
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Adequately addressed
1.8 14.9% dropped out of whole sample
1.9 Adequately addressed
1.10 Adequately addressed

Overall Assessment of the Study:
2.1 1+
2.2 in favour of treatment
2.3 yes
2.4 yes

LOEWENSTEIN2004

Data Used
MMSE
Notes: MMSE - translated into Cantonese

LAII2004

Study Type: RCT (individual)

Blindness: Single blind
Duration (days): Mean 42

Setting: 2 publically funded nursing homes in Hong Kong

Info on Screening Process: 127 screened, 26 excluded (mainly due to issues of consent or being hospitalized during recruitment) 15 dropped out during study (no longer wished to participate, later found not to meet inclusion criteria, death, hospitalized)

n= 101
Age: Mean 86
Sex: 32 males 69 females

Diagnosis:
- 100% Unspecified dementia by DSM IV

Exclusions: Not able to communicate most of the time; not able to speak and understand Cantonese; any active major psychiatric disorders (e.g. schizophrenia, major affective disorders); any acute or unstable chronic medical conditions (e.g. cardiac or lung diseases, blindness, deafness)

Baseline: Intervention group: MMSE = 8.3, MDS-ADL = 22.2, Social Engagement scale = 3.6, Well Being/Ill being scale = 1.3; Comparison Group: MMSE = 9.3, MDS-ADL = 21.6, Social Engagement scale = 3.4, Well being/Ill being = 1.3; Control group: MMSE = 10.7, MDS-ADL = 20.9, Social Engagement scale = 3.6, Well being/Ill being = 1.3

Group 1 N= 36
Reminiscence Therapy with - Weekly 30 minute session for 6 weeks. Highly focused use of triggers that approximate the life history of an individual and efforts to simulate recall during conversations

Group 2 N= 35
Social contact with - Weekly 30 minute sessions for 6 weeks. All features same as the reminiscence condition except facilitated not to discuss their life experiences. Themes of discussion included diet and health, and social security for the elderly

Group 3 N= 30
No treatment with
### Study Type: RCT (individual)

**Blindness:** Single blind  
**Duration (days):** Mean 98  
**Followup:** 3 months  
**Setting:** Mildly impaired people with AD in the US

#### Data Used

**Bill Paying:** Balancing a Checkbook task  
**Modified Making-Change for a Purchase Task:** Face-Name Association Task  
**Notes:** Bill Paying and Modified Making Change Tasks were modified from the Direct Assessment of Functional Status

#### Notes:
- N = 25: Cognitive rehabilitation with - 24 sessions twice per week for a period of 12-16 weeks: Learning face-name associations by SRT and dual cognitive support; practicing time-and-place orientation; activating procedural memory; practicing everyday activities (e.g. paying bills)

#### Group 1 N = 25
- Active control with - administered individually: commercially available computer games that matched pairs of letters, number from memory; exercises such as hangman; finding words in an array of letters; 'topic of the day' where info from recent or remote past remembered

#### Setting: Residential home residents  
**Duration (days):** Mean 98  
**Blindness:** Single blind  
**Study Type:** RCT (individual)  
**Study Description:** Randomisation by minimisation method, with age and relationship to caregiver stratifying variables. Home staff & family aware of treatment allocation.

---

### Study Type: RCT (individual)

**Blindness:** Single blind  
**Duration (days):** Mean 84  
**Followup:** 6 weeks  
**Setting:** Residential home residents  
**Notes:** Assessors only partly blind to group allocation. Allocation concealment-unclear.

### Data Used

**Autobiographical Memory Interview**  
**Life Satisfaction Index**  
**Geriatric Depression Scale**  
**Notes:** Assessments were carried out immediately before and after the intervention period and at 6 week follow-up

#### Group 1 N = 8
- Reminiscence Therapy with - Ave.12 individual weekly sessions, following Haight's Life Review Experiencing Form (Haight 1992); a life story book was developed for each person in the intervention group, incorporating the person's own words, accompanied by appropriate pictures.

#### Group 2 N = 9
- No treatment with

---

### Study Type: RCT (individual)

**Blindness:** Single blind  
**Duration (days):** Mean 56  
**Setting:** Participants recruited through Alzheimer's Association, Alzheimer’s Disease Research Centre and public media, in the US

#### Data Used

**Memory and Behavior Problems Checklist**  
**Brief Symptom Inventory**  
**Marital Needs Satisfaction Scale**  
**Notes:** Memory outcomes were measured with unvalidated composite scales therefore not included.

#### Group 1 N = 21
- Memory Training with - 1 hour daily for 5 days each week over 8 weeks. Caregiver as intervening agent who helped cognitively stimulate patient though memory provoking, problem solving, and conversational fluency activities.

#### Group 2 N = 29
- Dyadic counselling with - problem (conflict) identification, stress reduction, anger/frustration management, communication enhancement, conflict resolution. Incorporated both CBT approach and learning problem solving skills.
<table>
<thead>
<tr>
<th>Group</th>
<th>N=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support with Dual supportive seminar groups: all participants initially met for 1.5 hours for intro. Remaining 7 sessions patients and their carers met separately for first hour and simultaneously for the last half hour to discuss specific topics.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N=16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day care with - Provided respite care and education/training opportunities for caregivers. Patients met for 4 hours/week and participated in activities: social time, exercise, and recreational sports, monthly outings. Caregivers met monthly in support group.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N=15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waitlist with - Waited 8 weeks before being randomized to 1 of the 4 interventions.</td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**

**Internal Validity:**

1.1 Adequately addressed
1.2 Adequately addressed
1.3 Not addressed
1.4 Adequately covered
1.5 Adequately covered
1.6 Not addressed
1.7 Poorly addressed
1.8 Not reported
1.9 Not reported
1.10 Not applicable

**Overall Assessment of the Study:**

2.1 1+
2.2 favours treatment
2.3
2.4 yes

**ROBB1986**

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: Open</td>
</tr>
<tr>
<td>Duration (days): Mean 270</td>
</tr>
<tr>
<td>Setting: 400 bed long-term care division of a large Veterans Administration Medical Center.</td>
</tr>
<tr>
<td>Info on Screening Process: 60 screened, 36 met eligibility criteria</td>
</tr>
</tbody>
</table>

**Data Used**

- Minimal Social Behavior Scale
- Philadelphia Geriatric Center Morale Scale
- Mental Status Questionnaire

**Group 1 N=9**

Validation Therapy with - Twice a week for 9 months. Subjects attended most sessions.

**Group 2 N=6**

Validation Therapy with - Were randomized to the validation therapy group but did not attend most sessions because of episodic acute illness or extremely disruptive behaviour during the meeting.

**Group 3 N=12**

No treatment with

**Results from this paper:**

**Internal Validity:**
### SPECTOR2003

**Study Type:** RCT (individual)

- **Type of Analysis:** Intention to treat
- **Blindness:** Single blind
- **Duration (days):** Mean 42
- **Setting:** Multi-centre: 23 centres (18 residential homes, 5 day centres)
- **Info on Screening Process:** No people screened = 292

**Participants:**
- **Group 1:** N = 115
  - Reminiscence Therapy with 14 sessions, for 45 minutes, twice a week over 7 weeks. Topics included money, word games, the present day and famous faces. RO board displaying both personal and orientation information. Included elements of reminiscence, and multisensory stimulation

**Results from this paper:**
- **Internal Validity:**
  - 1.1 well covered
  - 1.2 well covered
  - 1.3 well covered
  - 1.4 well covered
  - 1.5 adequately addressed
  - 1.6 adequately addressed
  - 1.7 well covered
  - 1.8 Treatment group = 16% drop out, Control group = 19%
  - 1.9 Well covered
  - 1.10 Poorly addressed

**Overall assessment of study:**
- 2.1 1++
- 2.2 yes
- 2.3 applicable

### THORGRIMSEN2002

**Study Type:** RCT (individual)

- **Study Description:** Randomised using sealed envelopes.
- **Blindness:** Single blind
- **Duration (days):** Mean 126

**Participants:**
- **Group 1:** N = 7
  - Reminiscence Therapy with 18 weekly session based on the standardised manual Reminiscing with People with Dementia - A Handbook for Carers. Slides, photos, music, dance, dramatising memories were all used as...
| Setting: Sessions conducted by Age Exchange, London, UK. Participants lived in the community. | TOSELAND1997 | WALLIS1983 |
| Setting: 4 nursing homes in USA | Data Used | Data Used |
| Info on Screening Process: Information not provided. | n= 88<br>Age: Mean 88<br>Sex: 22 males 66 females<br>Diagnosis: 100% Unspecified dementia<br>Exclusions: 22 drop outs - 18 died, 2 deteriorating health, 2 refused to continue<br>Notes: Clinical diagnosis obtained from their medical records<br>Baseline: MOSES: self care - validation = 16.54, social contact = 16.09, usual care = 15.70; disorientation - validation = 15.68, social contact = 16.09, usual care = 17.91, depression - validation = 10.64, social contact = 7.73, usual care = 8.78; irritation - validation = 5.36, social contact = 5.64, usual care = 5.22; withdrawal - validation = 14.05, social contact = 13.05, usual care = 14.43 | n= 38<br>Age: Mean 72 Range 38-95<br>Sex: 25 males 13 females<br>Diagnosis: Exclusions: Exclusions: not long stay resident at the ward, not demented and or not withdrawn, willing or able to attend occupational therapy or industrial therapy, not capable of some meaningful communication, blind<br>Notes: Used a version of the Chrichton modified by Woods (1979) |
| Data Used<br>Cohen-Mansfield Agitation Inventory Score MOSES | Data Used<br>RCPhysicians’ mental scale for the elderly Chrichton Scale |
| | Group 1 N= 31<br>Validation Therapy with - Beginning of session foster warm greetings, holding hands, singing songs. Second segment: reminiscing about past events related to topic of interest. Third segment: activity e.g. sing-along, poetry reading. Fourth segment: refreshments and goodbyes | Group 1 N= 18<br>Reality Orientation with - Duration: half an hour daily for 5 days a week for 3 months. Repetition of information on orientation in time and place, names of persons present and comments on immediate surroundings, the weather and names and uses of everyday objects. |
| Group 2 N= 4<br>Control with tools. | Group 2 N= 29<br>Active control with - Following a manual containing 54 activities in 8 categories: music, art, literature, writing, dance/exercise, holiday and event planning, discussion, other activities<br>Group 3 N= 28<br>Standard Care with - Continued to participate in regular social and recreational program offered by nursing home |
| Setting: 4 nursing homes in USA | Study Type: RCT (individual) | Study Type: RCT (individual) |
| Blindness: Single blind | Duration (days): Mean 365 | Duration (days): Mean 90 |
| Duration (days): Mean 365 | Setting: 6 wards in High Roids hospital, Yorkshire | Followup: 1 month after treatment ended |
| Setting: 4 nursing homes in USA | Followup: 1 month after treatment ended | Setting: 6 wards in High Roids hospital, Yorkshire |
| Info on Screening Process: Information not provided. | Followup: 1 month after treatment ended | Followup: 1 month after treatment ended |
| Info on Screening Process: Information not provided. | Followup: 1 month after treatment ended | Followup: 1 month after treatment ended |

Results from this paper:

Internal Validity:
1.1 Well covered
1.2 Not reported
1.3 Not addressed
1.4 Adequately covered
1.5 Adequately covered
1.6 Adequately covered
1.7 Adequately covered
1.8 Validity group = 26% Social contact group = 28% Usual care group = 21%
1.9 Not addressed
1.10 Adequately addressed

Overall Assessment of the Study
2.1 1+
2.2
2.3 yes
2.4 yes
All persons with < 20% attendance (n = 22) reasons were: death (6), physical illness (8), refusal (5), could never be found (2), visitors every day (1)

Notes: Participants diagnosed as either functional (n = 19) or organic (n = 19) - the functional group were comprised of people with schizophrenia and affective disorders (n = 19)
Baseline: Chrichton: Reality Orientation group = 57.4; Control: = 52.2

Results from this paper:

Internal Validity:
1.1 Adequately addressed
1.2 Adequately addressed
1.3 Not addressed
1.4 Adequately addressed
1.5 Adequately addressed
1.6 Poorly addressed
1.7 Well covered
1.8 Reality orientation group = 40% drop out; Control group = 30% drop out
1.9 Not addressed
1.10 Poorly addressed

Overall assessment of quality:
2.1 1+
2.2 either in favour of treatment or control
2.3
2.4 not directly applicable because half of all participants were not demented

WOODS1979

Study Type: RCT (individual)
Study Description: randomised to reality orientation or active control, also controls from another home for the elderly (these controls not randomised therefore not inc
Blindness: Single blind
Duration (days):
Followup: 20 weeks
Setting: Residents at homes for the elderly mentally infirm
Info on Screening Process: Information not provided

Data Used
Chrichton Scale
WMS-R

Group 1 N= 5
Reality Orientation with - 5 days a week, for 30 mins, led by care staff in a room equipped with blackboard, calendar, clock, scrap books etc. A daily personal diary entry of basic information followed by various group activities e.g. spelling games, dominoes, simplified bingo

Group 2 N= 5
Active control with - Run as a discussion group with staff encouraging each resident to participate. RO materials were not used but sessions occasionally closed with a game of dominoes

Group 3 N= 4
No treatment with - Residents from another nursing home (not randomised)
## Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDERSON2001</td>
<td>Not RCT</td>
</tr>
<tr>
<td>ARKIN1997</td>
<td>Not RCT</td>
</tr>
<tr>
<td>BAILLON2004</td>
<td>Number of participants per group not provided</td>
</tr>
<tr>
<td>BALDELLI1993</td>
<td>Outcomes not adequately validated</td>
</tr>
<tr>
<td>BECK1988</td>
<td>Not RCT</td>
</tr>
<tr>
<td>BERNHARDT2002</td>
<td>Not RCT</td>
</tr>
<tr>
<td>BRINKMAN1982</td>
<td>Not RCT</td>
</tr>
<tr>
<td>BRODATY1997</td>
<td>Not RCT</td>
</tr>
<tr>
<td>CHAPMAN2004</td>
<td>Cognitive rehabilitation not assessed alone</td>
</tr>
<tr>
<td>CHERRY2004</td>
<td>Not RCT</td>
</tr>
<tr>
<td>CITRIN1977</td>
<td>No randomization</td>
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<tr>
<td>CLARE2004</td>
<td>Not RCT</td>
</tr>
<tr>
<td>COENMIELI1991</td>
<td>No evidence of randomization</td>
</tr>
<tr>
<td>DEVREESE1998</td>
<td>n&lt;10 per arm</td>
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<tr>
<td>DEVREESE2001</td>
<td>Not RCT</td>
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<tr>
<td>ERMINIFUNFSCHIL1995</td>
<td>Not RCT</td>
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<td>GERBER1991</td>
<td>Unable to extract outcome data</td>
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<tr>
<td>GOLDSTEIN1982</td>
<td>Not all participants had dementia</td>
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<tr>
<td>GUNTER1991</td>
<td>Participants did not have dementia</td>
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<tr>
<td>HANLEY1981</td>
<td>Data needed for extraction not provided</td>
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<td>HARRIS1976</td>
<td>No evidence of randomisation</td>
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<tr>
<td>HEAD1990</td>
<td>Non RCT</td>
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<tr>
<td>HOCHHALTER2004</td>
<td>Not randomised</td>
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<td>HOGSTEL1979</td>
<td>Participants may not have dementia</td>
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<tr>
<td>ISRAEL1987</td>
<td>Participants did not have dementia</td>
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<td>ISRAEL1989</td>
<td>Participants did not have dementia</td>
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<td>JOHNSON1981</td>
<td>No randomisation</td>
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<tr>
<td>KIXMILLER2002</td>
<td>Non RCT</td>
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<tr>
<td>MCKIERNAN1990</td>
<td>Non RCT</td>
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<tr>
<td>METTIERI2001</td>
<td>Non RCT</td>
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<tr>
<td>ORTEN1989</td>
<td>Participants without clear dementia diagnosis</td>
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<td>REEVE1985</td>
<td>Non RCT</td>
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<td>REQUENA2004</td>
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<td>SCHREIBER1999</td>
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<td>SHEIKH1986</td>
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<td>YESAVAGE1981</td>
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<td>ZANETTI1995</td>
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<td>ZARIT1982</td>
<td>Diagnosis inadequate</td>
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<tr>
<td>ZEPELIN1981</td>
<td>No evidence of randomisation</td>
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References of Included Studies

BAINES1987 (Published Data Only)

BAKER2003 (Published Data Only)

BREUIL1994 (Published Data Only)

CAHINWEINER2003 (Published Data Only)

CORBEIL1999 (Published Data Only)

DAVIS2001 (Published Data Only)

FERRAR1O1991 (Published Data Only)

GOLDWASSER1987 (Published Data Only)

HEISS1994 (Published Data Only)

KOLTAI2001 (Published Data Only)

LAI2004 (Published Data Only)

LOEWENSTEIN2004 (Published Data Only)

MORGAN2000 (Unpublished Data Only)

QUAYHAGEN2000 (Published Data Only)

ROBB1986 (Published Data Only)
References of Excluded Studies

SPECTOR2003 (Published Data Only)

THORGRIMSEN2002 (Published Data Only)

TOSELAND1997 (Published Data Only)

WALLIS1993 (Published Data Only)

WOODS1979 (Published Data Only)

References of Excluded Studies

ANDERSON2001 (Published Data Only)

ARKIN1997 (Published Data Only)

BAILLON2004 (Published Data Only)

BALDELLI1993 (Published Data Only)

BECK1988 (Published Data Only)

BERNHARDT2002 (Published Data Only)

BRINKMAN1982 (Published Data Only)

BRODATY1997 (Published Data Only)

BRICKMAN1982 (Published Data Only)

CHERRY2004 (Published Data Only)

CITRIN1977 (Published Data Only)
### Table 5: Included/excluded studies table for the review of acetylcholinesterase inhibiting drugs or memantine for the treatment of cognitive symptoms of non-Alzheimer's dementia or MCI

#### Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Acetylcholinesterase inhibitors vs. placebo for DLB</th>
<th>Acetylcholinesterase inhibitors vs. placebo for MCI</th>
<th>Acetylcholinesterase inhibitors vs. placebo for VaD</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLACK2003</td>
<td>GAL-INT-11</td>
<td>BLACK2003</td>
</tr>
<tr>
<td>ORGOGOZO2002</td>
<td>GAL-INT-18</td>
<td>ERKINJUNTTI2002</td>
</tr>
<tr>
<td>WILCOCK2002</td>
<td>PETERSEN2005</td>
<td>WILKINSON2003</td>
</tr>
</tbody>
</table>

#### Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BLACK2003</strong></td>
<td>n= 603</td>
<td>Data Used</td>
<td>Group 1 N= 199</td>
<td>Memantine vs. placebo for VaD</td>
</tr>
<tr>
<td>Study Type: RCT (individual)</td>
<td>Age: Mean 74 Range 45-91</td>
<td>CIBIC</td>
<td>Placebo with - Single daily doses of matching placebo to ensure blinding</td>
<td></td>
</tr>
<tr>
<td>Study Description: Computer generated randomisation protocol used.</td>
<td>Sex: 333 males 270 females</td>
<td>ADAS-Cog</td>
<td>Group 2 N= 198</td>
<td></td>
</tr>
<tr>
<td>Allocation concealment not addressed. Parallel-group study.</td>
<td>Diagnosis:</td>
<td>Notes: CIBIC-plus.</td>
<td>Donepezil with - Mean dose 5mg - Single daily doses of donepezil 5mg</td>
<td></td>
</tr>
<tr>
<td>Blindness: Double blind</td>
<td>100% Vascular Dementia by NINCDS-AIREN</td>
<td>CIBIS used as reference for subsequent CIBIC-plus ratings.</td>
<td>Group 3 N= 206</td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 168</td>
<td>Exclusions: Diagnosis of VaD &lt;3 months, no clinical of</td>
<td></td>
<td>Donepezil with - Mean dose 10mg - Single daily doses of 5mg/d for the first 4 weeks and 10mg/d thereafter</td>
<td></td>
</tr>
<tr>
<td>Setting: Out-patients. Multi-centred - America, Australia, Canada, England.</td>
<td>radiological evidence of CVD, unstable or controlled by medication for &lt;3 months hypertension, diabetes mellitus or heart disease, hospitilized for stroke &lt;3 months, clinical or radiological evidence of neurodegenerative disorders other than VaD, dementia due to AD or other conditions not associated with CVD, MMSE &gt;26 or &lt;10, major depression or other psychiatric disorders, experience of a myocardial infarction within 3 months of enrollement, pregnancy, history of drug or alcohol abuse, known hypersensitivity to donepezil.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Info on Screening Process: 952 screened 349 screen failures (illness or AE, MMSE &lt;10 or &gt;26, imaging, laboratory, medications, withdrew consent, diagnosis of AD, other)</td>
<td>Baseline: ADAS-cog: 20.1 (placebo), 21.2 (5mg), 20.9 (10mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MMSE: 21.7 (placebo), 21.9 (5mg), 21.8 (10mg)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>CDR-SB: 6.1 (placebo), 6.4 (5mg), 6.1 (10mg)</td>
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<tr>
<td></td>
<td>ADFACS: 15.9 (placebo), 17.3 (5mg), 15.3 (10mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Well covered
- 1.3 Not addressed
- 1.4 Well covered
- 1.5 Well covered
- 1.6 Well covered
- 1.7 Well covered
ERKINJUNNTI2002

Study Type: RCT (individual)
Study Description: Randomisation code generated by the Janssen Research Foundation (ratio two to one for galantamine vs placebo). External allocation concealment.

Blindness: Double blind
Duration (days): Mean 180
Setting: Multi-Centred - undertaken in 10 countries
Info on Screening Process: 750 screened 158 excluded - did not meet inclusion criteria, withdrew consent, other reasons.

n= 592
Age: Mean 75  Range 40-90
Sex: 312 males  280 females

Diagnosis:
42% Vascular Dementia by NINCDS-AIREN
48% Alzheimer's disease by NINCDS-ADRDA

Exclusions: MMSE <10 or >25, ADAS-cog <12, no available info from carer on patients ADL, no evidence of relevant focal neurological signs consistent with previous stroke and cerebrovascular disease, no lesions associated with dementia, no relations b/tn cerebrovascular disease and dementia defined by onset of dementia within 3 months of recognised stroke or abrupt deterioration in cognitive function. Evidence of neurodegenerative disorders other than AD that may cause or contribute to dementia. Cognitive impairment resulting from cerebral trauma, hypoxic cerebral damage, vitamin deficiency, infections, cerebral neoplasia, mental retardation or olioephrenia. Concomitant cardiovascular disease thought likely to prevent completion of the study. Concomitant epilepsy or clinically sig. psychiatric, hepatic, renal, pulmonary, metabolic or endocrine disturbances. An active peptic ulcer. History of sig. drug or alcohol abuse. Received investigational medication within the previous 30 days.

Notes: Alzheimer's disease with cerebrovascular disease

Baseline: ADAS-cog: 24.1 (placebo), 22.3 (galantamine)
MMSE: 20.2 (placebo), 20.7 (galantamine)
NPI: 11.4 (placebo), 12.2 (galantamine)

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Adequately addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 Placebo 15.1%, 5mg 18.7%, 10mg 28.2%
1.9 Well covered
1.10 Not addressed

Overall assessment of the study:
2.1 1+
2.2 Increase the effect of donepezil
2.3 Yes
2.4 Yes

Data Used
CIBIC
ADAS-Cog
Notes: CIBIC-plus

Group 1  N= 396
Galantamine with . Mean dose 24mg - Started on 4mg/day in the first week, with weekly increment of 4mg/day until they reached 24 mg/day in week 6. Administered as single tablets taken orally twice daily.

Group 2  N= 196
Placebo with - Administered as identical single tablets taken orally twice daily.
### GAL-INT-11

**Study Type:** RCT (individual)
**Study Description:** No details of randomisation or allocation concealment.
**Type of Analysis:** ITT
**Blindness:** Double blind
**Duration (days):** Mean 730

**Setting:** Austria, Canada, Finland, France, Germany, Netherlands, Poland, Sweden, Great Britain, US

**Info on Screening Process:** 780 subjects planned for enrolment with 995 randomised.

---

**Data Used**

- Diagnosis of dementia
- ADAS-Cog

**Group 1**

- N = 442
- Galantamine with Mean dose 8-12 mg - 4 weeks of 4mg twice daily, followed by 4 weeks of 8mg twice daily. Could be increased to 12 mg twice daily at month 2 and could be reduced to 8mg twice daily at month 3. Dose at month 3 was then fixed.

**Group 2**

- N = 452
- Placebo with - Matching placebo

---

### GAL-INT-18

**Study Type:** RCT (individual)
**Study Description:** No details of randomisation or allocation concealment.
**Type of Analysis:** ITT
**Blindness:** Double blind
**Duration (days):** Mean 730

**Setting:** Argentina, Australia, Belgium, Canada, Czech Republic, Israel, Spain, US.

**Info on Screening Process:** 780 subjects planned for enrolment with 1062 randomised.

---

**Data Used**

- Diagnosis of dementia
- ADAS-Cog

**Group 1**

- N = 498
- Galantamine with Mean dose 8-12mg/day - 4 weeks of 4mg twice daily, followed by 4 weeks of 8mg twice daily. Could be increased to 12 mg twice daily at month 2 and could be reduced to 8mg twice daily at month 3. Dose at month 3 was then fixed.

**Group 2**

- N = 511
- Placebo with - Matching placebo

---

### MCKEITH2000C

**Study Type:** RCT (individual)
**Study Description:** Randomisation list computer generated with proprietary computer app., acc. to randomised block design.
**Allocation concealment - sealed envelope.**
**Blindness:** Double blind
**Duration (days):** Mean 140

**Followup:** 3 weeks

**Setting:** Recruited from dementia assessment clinics in Spain, UK and Italy

**Info on Screening Process:** Not stated

---

**Data Used**

- CGC-plus
- MMSE
- NPI

**Group 1**

- N = 59
- Rivastigmine with Mean dose 6mg - Started with 1.5mg given twice a day. Doses were escalated by 1.5mg twice daily for a maximum of 2 weeks at each dose until 6mg twice daily or a maximum well tolerated maintenance dose was reached. Titration lasted up to 8 weeks.

**Group 2**

- N = 61
- Placebo with - As rivastigmine, plus, rivastigmine and placebo were presented in identical yellow capsules, size 2, and supplied in duplex blister packs containing 20 capsules for morning and evening administration over 10 days.

---

**Results from this paper:**

**Internal Validity:**
ORGOGOZO2002

Study Type: RCT (individual)
Study Description: No details of how the participants were randomised or allocation concealment.

Blindness: Double blind
Duration (days): Mean 196
Setting: 48 centres in France, 1 centre each in Belgium and Switzerland.

Info on Screening Process: 403 screened, 82 excluded for violation of inclusion/exclusion criteria, with lab values and CT/MRI scans being the most frequent reasons. So 321 randomly allocated of which 288 had at least 1 post baseline efficacy assessment.

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Not addressed
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 100% Vascular Dementia by NINCDS-AIREN
1.9 Not addressed
1.10 Not reported

Overall Assessment of the Study:
2.1 1+
2.2 1++
2.3 Yes
2.4 Yes

Data Used
- MMSE
- CIBIC
- ADAS-Cog

Group 1  N= 147
- Memantine with . Mean dose 20mg - After initial 3-week titration period with 5 mg/d at week 1, 10 mg/d at week 2, and 15 mg/d at weeking 3, patients received daily doses of 20 mg/d of memantine for the remainder of the 28 weeks follow up.

Group 2  N= 141
- Placebo with - Matching placebo to Mementine

PETERSEN2005

Table:

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N= 147</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memantine with . Mean dose 20mg - After initial 3-week titration period with 5 mg/d at week 1, 10 mg/d at week 2, and 15 mg/d at weeking 3, patients received daily doses of 20 mg/d of memantine for the remainder of the 28 weeks follow up.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2</th>
<th>N= 141</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo with - Matching placebo to Mementine</td>
<td></td>
</tr>
</tbody>
</table>

n= 288
Age: Mean 76
Sex: 152 males 136 females

Exclusions: <60yrs, <6 months of symptomatic mild to moderate VaD, MMSE <12 or >20. AD and secondary types of dementia. History of seizures, alcoholism, and/or drug abuse. Chronic users of other medications with the potential to interfere with the study outcomes and patients suffering from psychotic episodes. CT or MRI scan not showing vascular lesions in the brain or laboratory values outside the predetermined ranges.

Baseline: ADAS-COG: Memantine = 20.6, Placebo = 21.5
MMSE: Memantine = 16.9, Placebo = 16.9
**Study Type:** RCT (individual)

**Study Description:** Multicenter, randomised, double-blind, placebo-controlled parallel-group study. No details of randomisation or allocation concealment.

**Blindness:** Double blind

**Duration (days):** Mean 1096

**Setting:** ADCS sites in the US and Canada

**Info on Screening Process:** No information

---

**Data Used**

**Time to develop AD**

**Group 1**

- N = 253
- Donepezil with . Mean dose 10mg - 10mg of donepezil, placebo vitamin E, and a multivitamin daily. Initial dose was 5mg daily, increased to 10mg after 6 weeks.

**Group 2**

- N = 257
- Vitamin E with . Mean dose 2000 IU - 2000 IU of vitamin E, placebo donepezil, and a multivitamin daily. Initial dose was 1000 IU daily, increased to 2000 IU (1000 IU twice daily) after 6 weeks.

**Group 3**

- N = 259
- Placebo with - placebo vitamin E, placebo donepezil and a multivitamin daily.

---

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Not reported
- 1.3 Not addressed
- 1.4 Well covered
- 1.5 Well covered
- 1.6 Well covered
- 1.7 Well covered
- 1.8 32% in total dropped out
- 1.9 Well covered
- 1.10 Not addressed

**Overall assessment of the study:**
- 2.1 1
- 2.2 Increase the effect of treatment
- 2.3 Not sure
- 2.4 Yes

---

**SALLOWAY2004**

**Study Type:** RCT (individual)

**Study Description:** 24-week multicenter, randomised, double-blind, placebo controlled study. No details of allocation concealment, randomised in a 1:1 ratio.

**Blindness:** Double blind

**Duration (days):** Mean 168

**Setting:** Conducted at 22 study centers in the US. P’s had to be living independently.

**Info on Screening Process:** 588 screened. 284 did not meet entrance criteria, 19 withdrew consent, 15 failed screening for other reasons. 270 were randomised.

---

**Data Used**

**ADCS-CGIC**

**NY Uni Paragraph Test Delayed Recall**

**Group 1**

- N = 132
- Donepezil with . Mean dose 10mg - Administered orally each evening prior to bedtime. Received 5mg daily for 42 days, followed by 10 mg daily for the remainder of the study.

**Group 2**

- N = 137
- Placebo with - Administered orally each evening prior to bedtime.

---

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Not reported
- 1.3 Not addressed
- 1.4 Well covered
- 1.5 Well covered
- 1.6 Well covered
- 1.7 Well covered
- 1.8 32% in total dropped out
- 1.9 Well covered
- 1.10 Not addressed

**Overall assessment of the study:**
- 2.1 1
- 2.2 Increase the effect of treatment
- 2.3 Not sure
- 2.4 Yes
Internal Validity:
1.1 Well covered
1.2 Not reported
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Adequately addressed
1.8 Donepezil = 32.3%, Placebo = 16.8%
1.9 Well covered
1.10 Not addressed

Overall Assessment of the Study
2.1 1-
2.2 Favour treatment
2.3 No
2.4 Yes

WILCOCK2002

Study Type: RCT (individual)
Study Description: Balanced randomisation generated by SAS statistical software was carried out in 3 steps (in blocks of 4) by statistician with (continued in the notes)
Blindness: Double blind
Duration (days): Mean 196
Setting: UK day care or outpatients. Sites asked to adhere to testing at same daytime & setting whenever possible. Raters trained to standardise ratings.
Info on Screening Process: 844 screened 265 excluded
Reasons not given

n= 579
Age: Mean 77 Range 54-97
Sex: 298 males 281 females

Data Used
CGI-C
ADAS-Cog

Group 1 N= 295
Memantine with. Mean dose 20mg - Patients titrated up to a daily dose of 20mg starting at 5mg daily with weekly increments of 5 mg thus reaching 20mg in week 4. Daily maintenance dose fixed at 20mg memantine orally. Dosage split to 10mg b.i.d. in the morning and afternoon.

Group 2 N= 284
Placebo with - Identical taste and appearance to Memantine tablets

Cont. . . No access to information on the patients or physicians. Patients, investigating staff, and the Merz study team were blinded to treatment allocation until data base lock.

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Well covered
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 19% memantine, 20% placebo
1.9 Well covered
1.10 Adequately addressed

Overall assessment of the study:
2.1 1++
2.2
2.3 Yes
2.4 Yes

WILKINSON2003

n= 579
Age: Mean 77 Range 54-97
Sex: 298 males 281 females

Data Used
CGI-C
ADAS-Cog

Group 1 N= 295
Memantine with. Mean dose 20mg - Patients titrated up to a daily dose of 20mg starting at 5mg daily with weekly increments of 5 mg thus reaching 20mg in week 4. Daily maintenance dose fixed at 20mg memantine orally. Dosage split to 10mg b.i.d. in the morning and afternoon.

Group 2 N= 284
Placebo with - Identical taste and appearance to Memantine tablets

Cont. . . No access to information on the patients or physicians. Patients, investigating staff, and the Merz study team were blinded to treatment allocation until data base lock.

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Well covered
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 19% memantine, 20% placebo
1.9 Well covered
1.10 Adequately addressed

Overall assessment of the study:
2.1 1++
2.2
2.3 Yes
2.4 Yes
Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>AARSLAND2002</td>
<td>Small cross-over trial</td>
</tr>
<tr>
<td>ALLAIN2004</td>
<td>Review</td>
</tr>
<tr>
<td>BEGLINGER2005</td>
<td>Participants were healthy adults, ie, non-demented</td>
</tr>
<tr>
<td>DOODY2004</td>
<td>Not an RCT, open-label trial extension.</td>
</tr>
<tr>
<td>EDWARDS2004</td>
<td>Not an RCT, open-label study</td>
</tr>
<tr>
<td>EMRE2004</td>
<td>PD with dementia</td>
</tr>
<tr>
<td>ERKINJUNTTI2003B</td>
<td>Non RCT, open label extension</td>
</tr>
<tr>
<td>GAL-MCI-301</td>
<td>Non RCT</td>
</tr>
<tr>
<td>GOLOMB2004</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>IHL2003</td>
<td>Review</td>
</tr>
</tbody>
</table>

Data Used

- CIBIS
- CIBIC-plus
- ADAS-Cog

Study Type: RCT (individual)

Study Description: Computer generated randomisation protocol used.

Blindness: Double blind

Duration (days): Mean 168

Setting: Conducted at 51 sites in the US, Europe, Canada and Australia.

Info on Screening Process: 867 screened 271 excluded

Setting: Donepezil with . Mean dose 10mg - Received donepezil 5 mg/day for 4 weeks and then single daily dose of 10mg each evening before bedtime until week 24. Blinding ensured by use of identical-appearing placebo and donepezil tablets.

Setting: Donepezil with . Mean dose 5mg - Single daily dose of 5 mg taken each evening before bedtime.

Setting: Placebo with - Single daily dose taken each evening before bedtime. Identical-appearing tablets.

Results from this paper:

Baseline: ADAS-cog: Placebo = 18.8, Donepezil 5mg = 20.8, Donepezil 10mg = 20.6

MMSE: Placebo = 22.2, Donepezil 5mg = 21.8, Donepezil 10mg = 21.5

Internal Validity:

1.1 Well covered
1.2 Well covered
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 16.6% placebo, 19.2% donepezil 5mg, 24.7% donepezil 10mg
1.9 Well covered
1.10 Not reported

Overall assessment of the study:

2.1 1+
2.2 Increase the effect of treatment
2.3 Not sure
2.4 Yes
<table>
<thead>
<tr>
<th>Reference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BLACK2003</strong></td>
<td>Published Data Only</td>
</tr>
<tr>
<td><strong>ERKINJUNTTI2002</strong></td>
<td>Published Data Only</td>
</tr>
<tr>
<td><strong>GAL-INT-11</strong></td>
<td>Unpublished Data Only</td>
</tr>
<tr>
<td><strong>GAL-INT-18</strong></td>
<td>Unpublished Data Only</td>
</tr>
<tr>
<td><strong>MCKEITH2000C</strong></td>
<td>Published Data Only</td>
</tr>
<tr>
<td><strong>ORGOGOZO2002</strong></td>
<td>Published Data Only</td>
</tr>
<tr>
<td><strong>PETERSEN2005</strong></td>
<td>Published Data Only</td>
</tr>
<tr>
<td><strong>SALLOWAY2004</strong></td>
<td>Published Data Only</td>
</tr>
</tbody>
</table>

**References of Included Studies**

- **BLACK2003** (Published Data Only)
- **ERKINJUNTTI2002** (Published Data Only)
- **GAL-INT-11** (Unpublished Data Only)
- **GAL-INT-18** (Unpublished Data Only)
- **MCKEITH2000C** (Published Data Only)
- **ORGOGOZO2002** (Published Data Only)
- **PETERSEN2005** (Published Data Only)
- **SALLOWAY2004** (Published Data Only)
References of Excluded Studies

WILCOCK2002  (Published Data Only)

WILKINSON2003  (Published Data Only)

References of Excluded Studies

AARSLAND2002  (Published Data Only)

ALLAIN2004  (Published Data Only)

BEGLINGER2005  (Published Data Only)

DOODY2004  (Published Data Only)

EDWARDS2004  (Published Data Only)

EMRE2004  (Published Data Only)

ERKINJUNTI2003B  (Published Data Only)

GAL-MCI-301  (Unpublished Data Only)
An open-label extension study to assess the long-term safety and tolerability of galantamine HBr in the treatment of MCI.

GOLD2004  (Published Data Only)

GOLOMB2004  (Published Data Only)

IHLL2003  (Published Data Only)

JELIC2003  (Published Data Only)

KOONTZ2005  (Published Data Only)


Table 6: Included/excluded studies table for the review of medicine other than acetylcholinesterase inhibiting drugs or memantine for the treatment of cognitive symptoms of dementia

<table>
<thead>
<tr>
<th>Characteristics of Included Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
</tr>
<tr>
<td>AKHONDZADEH2003</td>
</tr>
<tr>
<td>Results from this paper:</td>
</tr>
<tr>
<td>Internal Validity:</td>
</tr>
<tr>
<td>1.1 Well covered</td>
</tr>
<tr>
<td>1.2 Well covered</td>
</tr>
<tr>
<td>1.3 Well covered</td>
</tr>
<tr>
<td>1.4 Well covered</td>
</tr>
<tr>
<td>1.5 Well covered</td>
</tr>
<tr>
<td>1.6 Well covered</td>
</tr>
<tr>
<td>1.7 Well covered</td>
</tr>
<tr>
<td>1.8 Dropout rates: 21% Salvia, 25% placebo</td>
</tr>
<tr>
<td>1.9 Adequately addressed</td>
</tr>
<tr>
<td>1.10 Not addressed</td>
</tr>
<tr>
<td>Overall Assessment of the Study</td>
</tr>
<tr>
<td>2.1 1++</td>
</tr>
<tr>
<td>2.2</td>
</tr>
<tr>
<td>2.3 Yes</td>
</tr>
<tr>
<td>2.4 Yes</td>
</tr>
</tbody>
</table>

| VAN2003 | | | | |
| Results from this paper: |
| Internal Validity: |
| 1.1 Well covered |
| 1.2 Well covered |
| 1.3 Not addressed |
| 1.4 Well covered |
| 1.5 Well covered |
| 1.6 Well covered |
| 1.7 Well covered |
| 1.8 Dropout rates: 11% gingko 240mg, 6% gingko 160mg, 8% placebo |
| 1.9 Well covered |
| 1.10 Not addressed |
| Overall Assessment of the Study |
| 2.1 1+ |

| WINBLAD2001A | | | | |
| Methods | Participants | Outcomes | Interventions | Notes |
Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Not addressed
1.4 Well covered
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Well covered
1.8 16.4% nicergoline, 18.9% placebo
1.9 Well covered
1.10 Not addressed
Overall assessment of the study:
2.1 1+

References of Included Studies

AKHONDZADEH2003 (Published Data Only)

VAN2003 (Published Data Only)

WINBLAD2001A (Published Data Only)
### Table 7: Included/excluded studies table for the review of psychosocial interventions for the management of behaviour that challenges

#### Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANCOLISRAEL2003A</strong>&lt;br&gt;Study Type: RCT (individual)&lt;br&gt;Ballard2002&lt;br&gt;Smallwood2001&lt;br&gt;Study Description: Cross-over trial + no treatment group&lt;br&gt;Blindness: No mention&lt;br&gt;Duration (days): Mean 10&lt;br&gt;Followup: 5 days&lt;br&gt;Setting: Nursing home residents in USA</td>
<td>n= 92&lt;br&gt;Age: Mean 82&lt;br&gt;Sex: 29 males 63 females&lt;br&gt;Diagnosis: 100% Alzheimer’s disease by NINCDS-ADRDA&lt;br&gt;Exclusions: No diagnosis of probable or possible AD, had a recent or severe stroke, had a primary psychiatric disorder which pre-dated suspected onset of their dementia, not agitated (in morning, evening or both)&lt;br&gt;Baseline: MMSE: 5.7</td>
<td>Data Used&lt;br&gt;Percentage sleep&lt;br&gt;Total Sleep Time&lt;br&gt;Notes: Used Actillume recorder to measure sleep. Movement recorded with a linear accelerometer and a microprocessor. Activity data were scored to determine wake and sleep based on both maximum and minute-by-minute activity</td>
<td>Group 1 N= 30&lt;br&gt;Light Therapy with - Morning bright light exposure. Apollo “Brite-Lite” boxes were used, they use cool-white fluorescent non-UV full spectrum light bulbs with a special ballast to augment brightness. The lights are shielded to limit ultraviolet and radio frequency radiations.</td>
<td></td>
</tr>
<tr>
<td><strong>BAINES1987</strong>&lt;br&gt;Study Type: RCT (individual)&lt;br&gt;Baines1987&lt;br&gt;Lai2004&lt;br&gt;Thorgrimsen2002&lt;br&gt;Study Description: Cross-over trial + no treatment group&lt;br&gt;Blindness: No mention&lt;br&gt;Duration (days): Mean 56&lt;br&gt;Setting: Residents of a large local authority home in UK with moderate/severe impairment of cognitive function</td>
<td>n= 15&lt;br&gt;Age: Mean 82&lt;br&gt;Sex: 1 male 14 females&lt;br&gt;Diagnosis:</td>
<td>Data Used&lt;br&gt;Behaviour Rating Scale (CAPE)&lt;br&gt;Mental ability (CAS)&lt;br&gt;Information/orientation (CAS)</td>
<td>Group 1 N= 5&lt;br&gt;Reality Orientation with - Group met for 30 mins/day Monday-Friday for 4 weeks. Used a large board for recording day, month, weather, writing materials, old newspapers etc. Also used materials to stimulate all 5 senses (e.g. distinctive smells, vials of rose water).</td>
<td></td>
</tr>
</tbody>
</table>
Baseline: Group A: information/orientation = 5.4, mental ability = 6.8; Group B: information/orientation = 5.8, mental ability = 8.2; Group C (control): information/orientation = 5.9, mental ability = 7.4

Reminiscence Therapy with - Group met for 30 mins/day Monday-Friday for 4 weeks. Set of 6 audio/slide programmes used to facilitate reminiscence from Help the Aged, old photographs of local scenes, residents' personal photos, books, magazines, newspapers

Group 2 N= 5
Reminiscence Therapy with - Group met for 30 mins/day Monday-Friday for 4 weeks. Set of 6 audio/slide programmes used to facilitate reminiscence from Help the Aged, old photographs of local scenes, residents' personal photos, books, magazines, newspapers

Reality Orientation with - Group met for 30 mins/day Monday-Friday for 4 weeks. Used a large board for recording day, month, weather, writing materials, old newspapers etc. Also used materials to stimulate all 5 senses (e.g. distinctive smells, vials of rose water)

Group 3 N= 5
No treatment with

Info on Screening Process: 20 screened: 3 excluded because of communication problems, 2 excluded because they didn't have cognitive impairment

No treatment with

Baseline: MMSE: UK MSS group = 8.8, Activity group = 6.5; Netherlands MSS group = 12.1, Activity group = 7.8, p=.05; Centres combined MSS group = 9.4, Activity group = 6.7, p=.01; GIP (Netherlands only): MSS group = 44.6, Activity group = 53.6, p<.05

Multi-sensory stimulation with - 8 standardized sessions (duration of 30 minutes), for 4 weeks, twice a week. Non-directive and enabling, special effects to stimulate all senses except taste, unpatterned non-sequential stimuli, no intellectual demands

Followup: One month after sessions

Setting: Multi-centre trial: UK (patients of a day hospital), Netherlands (residents of a psychogeriatric ward), Sweden (residents of a psychogeriatric ward)

Type of Analysis: Intention to treat

Blindness: Open

Followup: One month after sessions

Study Type: RCT (individual)

Duration (days): Mean 30

Followup: One month after sessions

Setting: Multi-centre trial: UK (patients of a day hospital), Netherlands (residents of a psychogeriatric ward), Sweden (residents of a psychogeriatric ward)

Info on Screening Process: 20 participants from Netherlands sample excluded before randomization: 8 transferred to another ward, 5 died, 3 not given informed consent, 4 carers did not respond to original letter

Baseline: MMSE: UK MSS group = 8.8, Activity group = 6.5; Netherlands MSS group = 12.1, Activity group = 7.8, p=.05; Centres combined MSS group = 9.4, Activity group = 6.7, p=.01; GIP (Netherlands only): MSS group = 44.6, Activity group = 53.6, p<.05

Data Used

REHAB
Behaviour and Mood Disturbance Scale
Behaviour Rating Scale (CAPE)
MMSE

Multi-sensory stimulation with - 8 standardized sessions (duration of 30 minutes), for 4 weeks, twice a week. Non-directive and enabling, special effects to stimulate all senses except taste, unpatterned non-sequential stimuli, no intellectual demands

Active control with - 8 standardized sessions (duration of 30 minutes), over 4 weeks, twice a week. Directive, no intended special multi-sensory experience, patterned often sequential stimuli, intellectual/physical demands specific to the task.
BALLARD2002

Study Type: RCT (cluster)
Blindness: Double blind
Duration (days): Mean 30
Setting: 8 NHS nursing homes
Info on Screening Process: Information not provided

n= 71
Age: Mean 79
Sex: 28 males  43 females
Diagnosis:
100% Unspecified dementia by Clinical Dementia Rating Scale
Exclusions: Exclusion criteria: agitation not clinically significant (as defined on the NPI), CDR < stage 3
Baseline: Active treatment: CMAI = 65; Placebo: CMAI = 58

Data Used
NPI
Cohen-Mansfield Agitation Inventory Score

Group 1 N= 35
Aromatherapy with - Treatment was twice daily, for 4 weeks. 10% (by weight) of Mellisa oil combined with base lotion (containing Prunus dulcis oil, glycerine, stearic acid, cetearyl alcohol, and tocopherl acetate). Lotion applied to the patient's face and both arms

Group 2 N= 36
Placebo with - Treatment was twice daily, for 4 weeks. 10% (by weight) of sunflower oil combined with base lotion (containing Prunus dulcis oil, glycerine, stearic acid, cetearyl alcohol, and tocopherl acetate). Lotion applied to the patient's face and both arms

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Adequately addressed
1.4 Well addressed
1.5 Adequately addressed
1.6 Poorly addressed
1.7 CMAI was not normally distributed, ANCOVA could not be used
1.8 Aroma therapy = 3% drop out; Placebo = 0% drop out
1.9 Not addressed
1.10 Adequately addressed

Overall Assessment of Study:
2.1 1+
2.2
2.3
2.4 yes

Summary:
CMAI not normally distributed so cannot be used in meta-analysis. Participants receiving aromatherapy significantly improved on the CMAI - 35% reduction in active treatment group vs 11% reduction in the placebo.

Conclusions: Both aromatherapy (35% reduction) and placebo (11% reduction) groups experienced significant improvements in agitation (CMAI)

DOWLING2005

Study Type: RCT (individual)
Blindness: No mention
Duration (days): Mean 77
Setting: Nursing home residents in the US

n= 70
Age: Mean 84  Range 58-98
Sex: 57 males  13 females
Diagnosis:
100% Alzheimer’s disease by NINCDS-ADRDA
Exclusions: inability to perceive light, not on stable medication, other neurological problems (e.g. Parkinson's Disease), regularly taking valerian, melatonin, sleep
Baseline: MMSE = 7

Data Used
Percentage sleep
Total Sleep Time

Group 1 N= 29
Light Therapy - morning with - Received morning (9:30-10:30am) bright light (>2500 lux in gaze direction) Monday-Friday for 10 weeks. During this time subjects participated in activities either outdoors or an indoor space with windows.

Group 2 N= 24
Light Therapy - afternoon with - Received afternoon (3:30-4:30pm) bright light (>2500 lux in gaze direction) Monday-Friday for 10 weeks. During this time subjects participated in activities either outdoors or an indoor space with windows.

Group 3 N= 17
Standard Care with

Results from this paper:
Internal Validity:
1.1 Adequately addressed
1.2 Not reported
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Adequately addressed
1.8
1.9 Not addressed
1.10 Not addressed

Overall Assessment of the Study:
2.1 1+
2.2 favours treatment
2.3 yes
2.4 yes

FERRARIO1991

Study Type: RCT (individual)
Blindness: No mention
Duration (days): Mean 168
Setting: Italy: institutionalized patients
Notes: Randomization not mentioned in paper but when contacted by Spector et al (2000) indicated it was randomized but gave no details of the method

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N= 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reality Orientation with - 1 hour formal session, 5 times a week. There was a 3 week break for Christmas and Easter holidays</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2</th>
<th>N= 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment with</td>
<td></td>
</tr>
</tbody>
</table>

Data Used
MOSES
Clifton Assessment Scale

Results from this paper:

Baseline:
- Treatment group: mean for CAS: information/orientation = 8.15, mental ability = 7.69, psychomotor performance = 7.69, total score = 23.54; mean MOSES: self care functioning = 19.15, disoriented behavior = 12.46, depressed anxious mood = 14.69, irritable behavior = 9.38, withdrawn behavior = 17.77
2.2 either direction
2.3 no
2.4 applicable but does not distinguish between types of dementia

**FONTANAGASIO2003**

**Study Type:** RCT (individual)

**Blindness:** No mention

**Duration (days):**

**Setting:** 2 nursing homes, 1 nursing wing of Psychiatric University Clinic Switzerland

**Info on Screening Process:** 7 excluded: 5 non compliance with wearing actimeter, 1 fear of intervention, 1 illness

Data Used
- Percentage sleep
- Total Sleep Time

Notes: rest-activity cycle measured by acti-watch worn on the non-dominant wrist. Sleep variable can then be calculated from this data.

1N = 9 Group
Light Therapy with - Dawn-dusk simulator (DDS) was used for 3 weeks. Two dates/latitudes chosen: Dusk on 10th April at 38 degrees N lasted 44 mins, the dark period 10h, the dawn 34 mins. Dusk on 1st July 29 degrees N lasted 30 mins, dark period 9h16mins, dawn 30 mins.

2N = 4 Group
Placebo with - Used the same simulation parameters but replaced the white light with red light

**Diagnosis:**
- Age: Mean 86 Range 78-95
- Sex: 4 males 9 females
- Diagnosis:
  - 69% Alzheimer's disease
  - 15% Vascular Dementia
  - 8% Dementia with Lewy Bodies
  - 8% Parkinson's Disease and dementia
- Exclusions: <65 years of age, no symptoms or diagnosis of dementia, no sleep problems, medical illness or other problems, blind or severely impaired vision

Baseline: MMSE: Treatment group = 13.8, Control group = 14.3

Results from this paper:

**Internal Validity:**
- 1.1 Well covered
- 1.2 Not reported
- 1.3 Not addressed
- 1.4 Not reported
- 1.5 Adequately addressed
- 1.6 Well covered
- 1.7 Well covered
- 1.8 0%
- 1.9 Adequately addressed
- 1.10 Poorly addressed

**Overall Assessment of the Study:**
- 2.1 1+
- 2.2 favours treatment
- 2.3 no
- 2.4 yes

**GROENE1993**

**Study Type:** RCT (individual)

**Blindness:** No mention

**Duration (days):** Mean 105

**Setting:** Major metropolitan health care facility on a special Alzheimer's Unit in the US, length of stay averaged 35 months, range of 1-150 months

Data Used
- MMSE

**Group 1 N=15**
Music therapy with - 5 sessions per week, over 15 weeks. Each session lasted 15 minutes. Involved listening to music, playing percussion instruments, singing, movement or dance. Live music was incorporated into each session (e.g strumming a guitar along with recorded music)

n=30
Age: Mean 78
Sex: 14 males 16 females
Diagnosis:
- Alzheimer's disease

- Placebo with - Used the same simulation parameters but replaced the white light with red light

**Group 2 N=4**

n=15
Age: Mean 86 Range 78-95
Sex: 4 males 9 females
Diagnosis:
- 69% Alzheimer's disease
- 15% Vascular Dementia
- 8% Dementia with Lewy Bodies
- 8% Parkinson's Disease and dementia
- 8% Parkinson's Disease and dementia
- Exclusions: <65 years of age, no symptoms or diagnosis of dementia, no sleep problems, medical illness or other problems, blind or severely impaired vision

Baseline: MMSE: Treatment group = 13.8, Control group = 14.3
<table>
<thead>
<tr>
<th>Notes: Wandering measured in terms of miles observed by staff per hour</th>
<th>Notes: Non-wandering measured in terms of time spent sitting down or in close proximity during intervention</th>
<th>Social contact with - Reading: 2 sessions a week, over 15 weeks. Each session lasted 15 minutes. Session involved reading aloud to a participant by the therapist or occasionally the participant reading aloud</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 N=17</td>
<td>Group 2 N=15</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Setting: Amsterdam, Netherlands residents of Bernadus Care Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Used</td>
</tr>
</tbody>
</table>

**GIP**

Gedragsobservatieschall voor de Intramurale Psychogeriatrie

<table>
<thead>
<tr>
<th>Exclusions: Did not exhibit wandering behaviour.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results from this paper:</td>
</tr>
<tr>
<td>Internal Validity:</td>
</tr>
<tr>
<td>1.1 Adequately covered</td>
</tr>
<tr>
<td>1.2 Adequately covered</td>
</tr>
<tr>
<td>1.3 Not addressed</td>
</tr>
<tr>
<td>1.4 Not reported</td>
</tr>
<tr>
<td>1.5 Not reported</td>
</tr>
<tr>
<td>1.6 Poorly addressed</td>
</tr>
<tr>
<td>1.7 Adequately addressed</td>
</tr>
<tr>
<td>1.8 Not reported</td>
</tr>
<tr>
<td>1.9 Not reported</td>
</tr>
<tr>
<td>1.10 Not applicable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall assessment of the Study:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 1+</td>
</tr>
<tr>
<td>2.2 either treatment or control</td>
</tr>
<tr>
<td>2.3 no</td>
</tr>
<tr>
<td>2.4 yes</td>
</tr>
</tbody>
</table>

**HOLTAKAMP1997**

Study Type: RCT (individual)

Study Description: Cross-over trial

Blindness: Single blind

Duration (days): Mean 10

Setting: Amsterdam, Netherlands residents of Bernadus Care Home

Info on Screening Process: Information not provided

<table>
<thead>
<tr>
<th>n=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 86 Range 79-97</td>
</tr>
<tr>
<td>Sex: 1 male 16 females</td>
</tr>
<tr>
<td>Diagnosis: 100% Unspecified dementia by DSM III-R</td>
</tr>
<tr>
<td>Exclusions: No diagnosis of dementia; inability to walk; inability to respond to non-verbal stimuli; inability to see or hear.</td>
</tr>
</tbody>
</table>

| Data Used |

**GIP**

Gedragsobservatieschall voor de Intramurale Psychogeriatrie

<table>
<thead>
<tr>
<th>Group 1 N=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-sensory stimulation with - 3 sessions in 3 consecutive days, lasting from 30 mins to an hour.</td>
</tr>
<tr>
<td>Standard Care with</td>
</tr>
</tbody>
</table>

Results from this paper:

Internal Validity:

1.1 Adequately addressed
1.2 Not reported
1.3 Not addressed
1.4 Adequately addressed
### LAI2004

**Study Type:** RCT (individual)

**Blindness:** Single blind

**Duration (days):** Mean 42

**Setting:** 2 publically funded nursing homes in Hong Kong

**Info on Screening Process:** 127 screened, 26 excluded (mainly due to issues of consent or being hospitalized during recruitment). 15 dropped out during study (no longer wished to participate, later found not to meet inclusion criteria, death, hospitalized).

**Baseline:**
- Intervention group: MMSE = 8.3, MDS-ADL = 22.2, Social Engagement scale = 3.6, Well being/Ill being scale = 1.3
- Comparison Group: MMSE = 9.3, MDS-ADL = 21.6, Social Engagement scale = 3.4, Well being/Ill being = 1.3
- Control group: MMSE = 10.7, MDS-ADL = 20.9, Social Engagement scale = 3.6, Well being/Ill being = 1.3

**Results from this paper:**

<table>
<thead>
<tr>
<th>Internal Validity</th>
<th>Adequately addressed</th>
<th>Adequately addressed</th>
<th>Not reported</th>
<th>Well covered</th>
<th>Adequately addressed</th>
<th>Adequately addressed</th>
<th>Adequately addressed</th>
<th>Adequately addressed</th>
<th>14.9% dropped out of whole sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Adequately addressed</td>
<td>Adequately addressed</td>
<td>Not reported</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Adequately addressed</td>
<td>Adequately addressed</td>
<td>Adequately addressed</td>
<td>14.9% dropped out of whole sample</td>
</tr>
<tr>
<td>2</td>
<td>1+</td>
<td>in favour of treatment</td>
<td>yes</td>
<td>yes</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>2+</td>
</tr>
</tbody>
</table>

**Overall Assessment of the Study:**
- 1+ (favourable)
- Yes
- Yes

**Conclusion:** There were less significantly less behavioral problems in the snoezelen group ($t = 8.99, p<.01$)

---

### LYKETSOS1999

**Study Type:** RCT (individual)

**Study Description:** Cross-over trial

**Type of Analysis:** Intention to treat - LOCF

**Data Used**
- **Behave-AD**
- **Cornell Scale for Depression in Dementia**

**Group 1 N=36**
- Reminiscence Therapy with - Weekly 30 minute session for 6 weeks. Highly focused use of triggers that approximate the life history of an individual and efforts to simulate recall during conversations

**Group 2 N=35**
- Social contact with - Weekly 30 minute sessions for 6 weeks. All features same as the reminiscence condition except facilitated not to discuss their life experiences. Themes of discussion included diet and health, and social security for the elderly

**Group 3 N=30**
- No treatment with...
<table>
<thead>
<tr>
<th>Results from this paper:</th>
<th>Internal Validity:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.1 Adequately addressed</td>
</tr>
<tr>
<td></td>
<td>1.2 Poorly addressed</td>
</tr>
<tr>
<td></td>
<td>1.3 Not reported</td>
</tr>
<tr>
<td></td>
<td>1.4 Adequately addressed</td>
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<tr>
<td></td>
<td>1.5 Adequately addressed</td>
</tr>
<tr>
<td></td>
<td>1.6 Adequately addressed</td>
</tr>
<tr>
<td></td>
<td>1.7 Adequately addressed</td>
</tr>
<tr>
<td></td>
<td>1.8 47% dropped out</td>
</tr>
<tr>
<td></td>
<td>1.9 Well covered</td>
</tr>
<tr>
<td></td>
<td>1.10 Not applicable</td>
</tr>
<tr>
<td>Overall Assessment of the Study:</td>
<td>2.1 1+</td>
</tr>
<tr>
<td></td>
<td>2.2 Favours treatment</td>
</tr>
<tr>
<td></td>
<td>2.3 no</td>
</tr>
<tr>
<td></td>
<td>2.4 yes</td>
</tr>
</tbody>
</table>

Conclusions: Statistically significant difference in nocturnal sleep hours between baseline and 4 weeks after light therapy (t [14] = 2.37, p<.05) but not after placebo. No significant difference between light therapy and placebo for nocturnal sleep hours. No significant effects on behavioural outcomes: Behave-AD, Cornell Depression Scale.
Conclusions: Participants with VaD experienced a statistically significant reduction in night time activity, and percentage of night time activity after BLT but not DLT. No significant differences for participants with AD.

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Not addressed
1.4 Poorly addressed
1.5 Adequately addressed
1.6 Poorly addressed
1.7 Poorly addressed
1.8 Experimental group = 25% Control group = 25% drop out
1.9 Poorly addressed
1.10 Not applicable

Overall Assessment of the Study:
2.1 1+
2.2 In favour of treatment
2.3 No
to some extent (but 25% of participants did not have dementia)
<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>Group 1 N=7</th>
<th>Group 2 N=7</th>
<th>Group 3 N=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness:</td>
<td>Aromatherapy with Massage with Massage with Conversation + aroma disseminated by diffuser with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration (days):</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THORGRIMSEN2002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type: RCT (individual)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Description: Randomised using sealed envelopes.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blindness: Single blind</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Duration (days): Mean 126</td>
<td></td>
<td></td>
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<tr>
<td>Setting: Sessions conducted by Age Exchange, London, UK. Participants lived in the community.</td>
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<tr>
<td>Info on Screening Process: Information not provided.</td>
<td></td>
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<tr>
<td>n=21</td>
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</tr>
<tr>
<td>Age: Mean 67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex: 9 males 12 females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified dementia by Consultant psychiatrist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data Used</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behaviour Rating Scale (CAPE)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
<td></td>
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<tr>
<td>QoL-AD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOSELAND1997</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type: RCT (individual)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Study Description:</td>
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</tbody>
</table>

| Data Used                    |             |             |             |
| Behaviour Rating Scale (CAPE) |             |             |             |
| MMSE                         |             |             |             |
| QoL-AD                       |             |             |             |
| Data Used                    |             |             |             |
| Cohen-Mansfield Agitation Inventory Score MOSES |             |             |             |

| Group 1 N=7                  | Reminiscence Therapy with - 18 weekly session based on the standardised manual Reminiscing with People with Dementia - A Handbook for Carers. Slides, photos, music, dance, dramatising memories were all used as tools. |
| Group 2 N=4                  | Control with |
| Group 3 N=7                  |             |             |             |

| Setting: 4 nursing homes in USA |             |             |             |
| Info on Screening Process: No. people screened = 126, excluded: 38; reasons: 33 severe dementia, 2 didn’t have clear dementia diagnosis, 2 discharged before groups began, 1 refused to attend |
| n=11                         |             |             |             |
| Age: Mean 77                 |             |             |             |
| Sex: 5 males 6 females       |             |             |             |
| Diagnosis:                   |             |             |             |
| 100% Unspecified dementia    |             |             |             |
| Exclusions:                  |             |             |             |
| 22 drop outs - 18 died, 2 deteriorating health, 2 refused to continue |
| Notes: Clinical diagnosis obtained from their medical records |
| Baseline: MOSES: self care - validation = 16.54, social contact = 16.09, usual care = 15.70; disorientation - validation = 15.68, social contact = 16.09, usual care = 17.91, depression - validation = 10.64, social contact = 7.73, usual care = 8.78; irritation - validation = 5.36, social contact = 5.64, usual care = 5.22; withdrawal - validation = 14.05, social contact = 13.05, usual care = 14.43 |             |             |             |

Results from this paper:

<table>
<thead>
<tr>
<th>Internal Validity:</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Well covered</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2 Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3 Not addressed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4 Adequately covered</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5 Adequately covered</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.6 Adequately covered</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.7 Adequately covered</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.8 Validity group = 26% Social contact group = 28% Usual care group = 21%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.9 Not addressed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.10 Adequately addressed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Overall Assessment of the Study
2.1 1+
2.2
2.3 yes
2.4 yes

WALLIS1983

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: Single blind</td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 90</td>
<td></td>
</tr>
<tr>
<td>Followup: 1 month after treatment ended</td>
<td></td>
</tr>
<tr>
<td>Setting: 6 wards in High Royds hospital, Yorkshire</td>
<td></td>
</tr>
<tr>
<td>Info on Screening Process: Information not provided</td>
<td></td>
</tr>
</tbody>
</table>

Data Used
RCPhysicians’ mental scale for the elderly
Chrichton Scale
Notes: Used a version of the Chrichton modified by Woods (1979)

Group 1 N= 18
Reality Orientation with - Duration: half an hour daily for 5 days a week for 3 months. Repetition of information on orientation in time and place, names of persons present and comments on immediate surroundings, the weather and names and uses of everyday objects.

Group 2 N= 20
Active control with - Duration: half an hour daily 5 days a week for 3 months. Variety of group and individual activities offered each day. Each patient choses their activity and groups subdivided according to this choice.

Results from this paper:
Internal Validity:
1.1 Adequately addressed
1.2 Adequately addressed
1.3 Not addressed
1.4 Adequately addressed
1.5 Adequately addressed
1.6 Poorly addressed
1.7 Well covered
1.8 Reality orientation group = 40% drop out; Control group = 30% drop out
1.9 Not addressed
1.10 Poorly addressed

Overall assessment of quality:
2.1 1+
2.2 either in favour of treatment or control
2.3
2.4 not directly applicable because half of all participants were not demented

Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABEGG1993</td>
<td>Not RCT</td>
</tr>
<tr>
<td>ALPRIN1980</td>
<td>can’t find paper</td>
</tr>
<tr>
<td>ANCOLIISRAEL1997</td>
<td>Not RCT</td>
</tr>
<tr>
<td>ANCOLIISRAEL2002</td>
<td>Not RCT</td>
</tr>
<tr>
<td>ASMUSSEN1997</td>
<td>can’t find report</td>
</tr>
<tr>
<td>BABINS1988</td>
<td>not RCT</td>
</tr>
<tr>
<td>BABINS1988A</td>
<td>not RCT</td>
</tr>
</tbody>
</table>
BAILLON2004
BESHARA2002 Not RCT
BLEATHMAN1988 Not RCT
BROTONS2000 incorrect form of analysis for cross-over data
BUXTON2005 Not RCT
CANON1996 Not RCT
CLAIR1993 not RCT
CLAIR1994 no standardized outcomes used
CLAIR1996 invalid outcomes
CLARK1998 no standardized outcomes used
COHENMANSFIELD1997 no RCT
COLENDL1997 Not RCT
COX2004 Not randomized
DAWSON1999 Not RCT
DOYLE1992 Not RCT
DYE1999 Not RCT
ESPERANZA1987 Not RCT
FEIL1972 Not RCT
FINE1995 Not RCT
FOSTER2001 not RCT
FRITZ1986 Non RCT
GERDNER2000 Incorrect form of analysis for cross-over data
GODDAER1994 not clear patients diagnosed with dementia
GÖTELL2003 No standardized outcomes used
GRAF2001 Only cognitive outcomes, no behavioural outcomes
HAFFMANS2001 Non RCT
HALPERN2000 Non RCT
HANSER1994 Participants did not have dementia
HANSON1996 Non RCT
HARRIS1995 Non RCT
HOLMES2002 Non RCT
HOZUMI1990 Non RCT
ITO1999 Non RCT
ITO2001 Non RCT
JACKSON2001 Cluster randomised trial without correct form of statistical analysis
JOHNS1991 Non RCT
KORB1997 Non RCT
KOYAMA1999 Non RCT
KUMAR1999 Did not contain required outcomes
LAGARCE2004 No standardised outcome measures used
LINDENMUTH1992 Non RCT
LORD1993 No standardised outcomes
LOVELL1995 Non RCT
MILLARD1989 Non RCT
MISHIMA1994 Non RCT
References of Included Studies

MISHIMA2000  Non RCT
MISKELLY2004  Non RCT
MITCHELL1993  n<10 per arm
MORTON1991  Non RCT
NEAL1994  Non RCT
OKAWA1989  Non RCT
OKAWA1993  Non RCT
OKAWA1999  Non RCT
OKUMOTO1998  Non RCT
OPIE1999  Non RCT
OTTO1999  Non RCT
PEOPLES1982  Can't locate reference
PINCOCK2003  Non RCT
PINKNEY1997  Non RCT
POMEROY1993  Not music therapy alone
PRETCZYNSKI1991  Non RCT
REMMINGTON2002  Participants not diagnosis with dementia
RHEAUME1998  Non RCT
RIEGLER1980  Not clear participants diagnosed with dementia
RIEMERSMA2001  Non RCT
RIEMERSMA2002  Non RCT
ROBICHAUD1994  Didn't meet inclusion criteria
RUGGIERO1997  Non RCT
SATLIN1992  Non RCT
SCANLAND1993  Non RCT
SHALEK2004  Didn't meet inclusion criteria
SHARP1989  Non RCT
SMITH1986A  Non RCT
SNOW1990  Non RCT
SNOW2004  Non RCT
SUZUKI2004  No evidence of randomisation
THORPE2000  Non RCT
TOMAINO1999  Cannot locate reference
VANDERARK1983  Not clear whether participants diagnosed with dementia
VANDIEPEN2002  Limited data available for analysis
VANESSENCOX1995  Non RCT
VANSONEREN1997  Non RCT
VANWEERTJULIA2005  Non RCT
WOODS1996  Did not use aromatherapy
YAMADERA2000  Non RCT
ZARIT1982  Inadequate diagnosis


References of Excluded Studies

THORGRIMSEN2002 (Published Data Only)

TOSELAND1997 (Published Data Only)

WALLIS1983 (Published Data Only)

References of Excluded Studies

ABEGG1993 (Published Data Only)

ALPRIN1980 (Unpublished Data Only)

ANCOLIISRAEL1997 (Published Data Only)

ANCOLIISRAEL2002 (Published Data Only)

ASMUSSEN1997 (Unpublished Data Only)

BABINS1988 (Published Data Only)

BABINS1988A (Published Data Only)

BAILLON2004 (Published Data Only)

BESHARA2002 (Published Data Only)

BLEATHMAN1988 (Published Data Only)
BLEATHMAN1988

BROTONS2000 (Published Data Only)

BUXTON2005 (Published Data Only)
Buxton, H. L. (2005). The effects of running a validation therapy group on staff-client interactions in a day centre for the elderly. University of East Anglia, Health Policy and Practice Unit.

CANON1996 (Published Data Only)
Canon, R. L. (1996). The effect of validation therapy training on satisfaction with communication and quality of relationship between primary caregivers and demented residents in long term care. University of Texas at Austin, US.
CLAIR1993 (Published Data Only)

CLAIR1994 (Published Data Only)

CLAIR1996 (Published Data Only)

CLARK1998 (Published Data Only)

COHEN-MANSFIELD1997 (Published Data Only)

COLEDA1997 (Published Data Only)

COX2004 (Published Data Only)

DAWSON1999 (Published Data Only)

DOYLE1992 (Published Data Only)

DYE1999 (Published Data Only)

ESPERANZA1987 (Published Data Only)
Esperanza, N. (1987). Validation therapy and remotivation as treatment for the confused institutionalized elderly. Rutgers University, Newark, USA.

FEIL1972 (Published Data Only)

FINE1995 (Published Data Only)

FOSTER2001 (Published Data Only)

FRITZ1986 (Published Data Only)

GERDNER2000 (Published Data Only)

GODDAER1994 (Published Data Only)

GÖTELL2003 (Published Data Only)
GRAF2001 (Published Data Only)

HAFFMANS2001 (Published Data Only)

HALPERN2000 (Published Data Only)

HANER1994 (Published Data Only)

HANSON1996 (Published Data Only)

HARRIS1995 (Published Data Only)

HOLMES2002 (Published Data Only)

HOZUMI1990 (Published Data Only)

ITO1999 (Published Data Only)

ITO2001 (Published Data Only)

JACKSON2001 (Unpublished Data Only)

JOHNS1991 (Published Data Only)

KORB1997 (Published Data Only)

KOYAMA1999 (Published Data Only)

KUMAR1999 (Published Data Only)

LAGARCE2004 (Published Data Only)

LINDENMUTH1992 (Published Data Only)
LORD1993

LOVELL1995

MILLARD1989

MISHIMA1994

MISHIMA2000

MISKELLY2004

MITCHELL1993

MORTON1991

NEAL1994
Neal, M. (1994). An Ethnographic study into the experience of Five Nurses who use Validation in their Interaction with Patients who have Senile Dementia. Nursing.

OKAWA1989

OKAWA1993

OKAWA1999

OKUMOTO1998

OPIE1999

OTTO1999

PEOPLES1982

PINCOCK2003

PINKNEY1997
THORPE2000 (Published Data Only)

TOMAINO1999 (Unpublished Data Only)

VANDERARK1983 (Published Data Only)

VANDEPEN2002 (Published Data Only)

VANESSENCOX1995 (Unpublished Data Only)

VAN SOMEREN1997 (Published Data Only)

VANWEERT JULIA2005 (Published Data Only)

WOODS1996 (Published Data Only)

YAMADERA2000 (Published Data Only)

ZARIT1982 (Published Data Only)

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### Table 8: Included/excluded studies table for the review of psychological interventions for co-morbid emotional disorders

#### Comparisons Included in this Clinical Question
- Psychological intervention vs 'standard care'

<table>
<thead>
<tr>
<th>Characteristics of Included Studies</th>
<th>Methods</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **BRODATY2003B**                    | Study Type: RCT (individual)  
Study Description: P’s randomly allocated using computer generated numbers. No mention of allocation concealment.  
Blindness: No mention  
Duration (days): Mean 84  
Setting: Recruited from 11 nursing homes in Sydney, Australia.  
Info on Screening Process: 647 residents screened, 561 excluded, see exclusions | n= 86  
Age: Mean 83  
Sex: 24 males 62 females  
Diagnosis:  
100% Unspecified dementia by DSM IV  
40% Depression by Hamilton Rating Scale for Depression  
38% Depression and Psychosis by Hamilton Rating Scale for Depression  
Exclusions: Inability to communicate, no consent given, resided in nursing home for less than a month, >7 on the AMTS, manifest less than 3 depressive symptoms on the BEHAVE-AD, did not reach predetermined cut-off criteria on at least 2 depression scales or psychosis scales.  
Baseline: Abbreviated Mental Test Score = 3.29  
Hamilton Rating Scale for Depression = 15.58 | Data Used  
Hamilton Depression Rating Scale | Group 1  
N= 40  
Psychogeriatric case management with - Psychosocial interventions for depression, 4-8 hrs over 12 weeks. Some pharmacotherpay according to standard clinical procedure. | Group 1  
N= 40  
Psychogeriatric consultation with - 12-week treatment phase |

| **TERI1997**                        | Study Type: RCT (individual)  
Study Description: Controlled clinical trial. No details of how p’s were randomised or allocation concealment.  
Blindness: No mention  
Duration (days): Mean 63  
Setting: P’s living with caregivers in the community, referrals from University of Washington Medical Center, US.  
Info on Screening Process: 88 patient-caregiver pairs began the study, 72 completed the study. Discontinuing reasons: serious medical illness (4), change in living situation (4), exclusionary medication prescribed during intervention stage (2), caregiver stopped participating (6) | n= 72  
Age: Mean 76  
Sex: 38 males 34 females  
Diagnosis:  
100% Alzheimer’s disease by NINCDS-ADRDA  
75% Major Depressive Disorder by DSM III-R  
25% Minor Depressive Disorder by DSM III-R  
Exclusions: Did not meet the NINCDS-ADRDA criteria for probable AD, less than 6 months history of cognitive problems, did not live with their caregiver within the | Data Used  
Cornell Scale for Depression in Dementia  
Hamilton Depression Rating Scale | Group 1  
N= 23  
Behaviour Therapy-Pleasant Events with - Taught strategies to increase pleasant events and alter contingencies relating to depression. Nine 60-min sessions once a week. Caregivers participated in varying degrees. | Group 2  
N= 19  
Behaviour Therapy-Problem-solving with - More caregiver input, used a systematic approach to problem-solving situations of concern. Provided education, advice and support for carers. Nine 60-min sessions once a week. |

**Group 3**  
N= 10  
Typical Care Control with - Typical advice and support usually provided within the community. Nine 60-min sessions once a week.
community, did not meet the RDC or DSM-III-R criteria for depression or have a Hamilton Depression Rating Scale score of at least 10.

Baseline: MMSE = 16.5
Beck Depression Inventory = 17.9

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waitlist with - Equal duration, no contact with therapists.</td>
<td></td>
</tr>
</tbody>
</table>

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Not addressed
1.3 Not addressed
1.4 Not addressed
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 18%
1.9 Not addressed
1.10 Not applicable

Overall assessment of the study:
2.1 Increase the effect of the interventions
2.2 No
2.3 Yes

Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABRAHAM1992</td>
<td>Participants did not have dementia</td>
</tr>
<tr>
<td>CHURCHILL1999</td>
<td>Non RCT</td>
</tr>
<tr>
<td>FRITZ1995</td>
<td>Non RCT</td>
</tr>
<tr>
<td>FRITZ1996</td>
<td>Non RCT</td>
</tr>
<tr>
<td>QAIZ2003</td>
<td>Non RCT</td>
</tr>
<tr>
<td>RAINA1999</td>
<td>Non RCT</td>
</tr>
<tr>
<td>SNOWDEN2003</td>
<td>Not comorbid, depression or dementia, not both</td>
</tr>
<tr>
<td>TORTA2004</td>
<td>Review</td>
</tr>
</tbody>
</table>

References of Included Studies

BRODATY2003B (Published Data Only)

Brodaty, H., Draper, B. M., Millar, J., Low, L. F., Lie, D., Sharah, S. et al. (2003). Randomized controlled trial of different models of care for nursing home residents with dementia complicated by depression or psychosis. Journal of Clinical Psychiatry., 64, Date.

TERI1997 (Published Data Only)


References of Excluded Studies

ABRAHAM1992 (Published Data Only)

CHURCHILL1999


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### Table 9: Included/excluded studies table for the review of pharmacological interventions for non-cognitive symptoms of dementia

#### Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Comparisons Included in this Clinical Question</th>
<th>Studies Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole vs. placebo for AD</td>
<td>CN 138-005, DEDEYN2005</td>
</tr>
<tr>
<td>Donepezil vs. galantamine for AD</td>
<td>WILCOCK2003</td>
</tr>
<tr>
<td>Donepezil vs. rivastigmine for AD</td>
<td>BULLOCK2005</td>
</tr>
<tr>
<td>Donepezil/ galantamine vs. placebo for VaD</td>
<td>BLACK2003, ERKINJUNTI2002, WILKINSON2003</td>
</tr>
<tr>
<td>Haloperidol vs. placebo for AD &amp; VaD</td>
<td>DEDEYN1999B</td>
</tr>
<tr>
<td>IM lorazepam vs. placebo</td>
<td>MEEHAN2002</td>
</tr>
<tr>
<td>IM olanzapine vs. placebo</td>
<td>MEEHAN2002</td>
</tr>
<tr>
<td>Memantine vs. placebo for AD</td>
<td>MD-01, MD-10/PESKIND2004, REISBERG2003A, TARIOT2004C</td>
</tr>
<tr>
<td>Olanzapine vs. placebo for AD &amp; VaD</td>
<td>DEBERDT2005, DEDEYN2004, F1D-MC-HGAO, STREET2000A</td>
</tr>
<tr>
<td>Quetiapine vs. placebo for AD &amp; VaD</td>
<td>BALLARD2005B</td>
</tr>
<tr>
<td>Rivastigmine vs. placebo for DLB</td>
<td>MCKEITH2000C</td>
</tr>
</tbody>
</table>

#### Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>BALLARD2005B</td>
<td>n = 93, Age: Mean 84, Sex: 19 males 74 females</td>
<td>Data Used: Cohen-Mansfield Agitation Inventory Score</td>
<td>Group 1 N=31 Quetiapine with - Aimed to attain doses of 25-50mg quetiapine twice a day by week 12 and doses of 50mg quetiapine twice a day between week 12 and 26.</td>
<td></td>
</tr>
</tbody>
</table>
**BLACK2003**

**Type of Analysis:** ITT  
**Blindness:** Double blind  
**Duration (days):** Mean 182  
**Setting:** Participants living in care facilities in Newcastle, UK.  
**Info on Screening Process:** 282 screened, 189 excluded - lack of consent, ineligible, death

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Placebo</th>
<th>Matching placebo</th>
<th>Rivastigmine with</th>
<th>Aimed to attain doses of 3-6 mg rivastigmine twice a day and doses of &gt;9 mg rivastigmine daily between week 12 and 26.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>199</td>
<td>Placebo with</td>
<td>Single daily doses of matching placebo to ensure blinding</td>
<td>2 N= 198</td>
<td>Donepezil with - Mean dose 5mg - Single daily doses of donepezil 5mg</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>Placebo with</td>
<td>-</td>
<td>Group 2 N= 31</td>
<td>Placebo with - Matching placebo</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>Placebo with</td>
<td>-</td>
<td>Group 3 N= 31</td>
<td>Rivastigmine with - Aimed to attain doses of 3-6 mg rivastigmine twice a day and doses of &gt;9 mg rivastigmine daily between week 12 and 26.</td>
</tr>
</tbody>
</table>

**Results from this paper:**

**Internal Validity:**
1.1 Well covered  
1.2 Well covered  
1.3 Well covered  
1.4 Well covered  
1.5 Well covered  
1.6 Well covered  
1.7 Adequately addressed  
1.8 33% rivastigmine, 25% quetiapine, 3% placebo  
1.9 Well covered  
1.10 Not applicable  

**Overall Assessment of Study:**
2.1 1++  
2.2  
2.3 yes  
2.4 yes

**Type of Analysis:** ITT  
**Blindness:** Double blind  
**Duration (days):** Mean 168  
**Setting:** Out-patients. Mult-centred - America, Australia, Canada, England.  
**Info on Screening Process:** 952 screened, 349 screen failures (illness or AE, MMSE <10 or >26, imaging, laboratory, medications, withdrew consent, diagnosis of AD, other)
Notes: 70.5% probable diagnosis
29.5% possible diagnosis
Baseline: ADAS-cog: 20.1 (placebo), 21.2 (5mg), 20.9 (10mg)
MMSE: 21.7 (placebo), 21.9 (5mg), 21.8 (10mg)
CDR-SB: 6.1 (placebo), 6.4 (5mg), 6.1 (10mg)
ADFACS: 15.9 (placebo), 17.3 (5mg), 15.3 (10mg)

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 Placebo 15.1%, 5mg 18.7%, 10mg 28.2%
1.9 Well covered
1.10 Not reported

Overall assessment of the study:
2.1 1+
2.2 Increase the effect of donepezil
2.3 Yes
2.4 Yes

Data Used
CGI-C
Behave-AD
Cohen-Mansfield Agitation Inventory Score

Brodaty2003C

Study Type: RCT (individual)
Study Description: Randomly assigned according to randomisation code that was balanced to ensure even dist. Of patients. Allocation concealment not mentioned.
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 84
Setting: 14 sites in Australia and NZ. Patients had to reside in a nursing home for at least 1 month prior to enrollment.
Info on Screening Process: 384 enrolled and entered washout period. 39 discontinued, 345 randomised to treatment
n= 345
Age: Mean 83
Sex: 123 males 222 females
Diagnosis:
52% Alzheimer’s disease by DSM IV
25% Vascular Dementia by DSM IV
12% Mixed Dementia by DSM IV
Exclusions: <55 years of age; >23 MMSE; medical or neurological conditions other than dementia that diminish cognitive function; major depression; other psychiatric disorders that could have accounted for observed psychotic disturbances; history of tardive dyskinesia; clinically uncontrolled organic disease; clinically relevant laboratory abnormalities.
Baseline: CMAI total aggression: 33.0 (placebo), 34.1 (risperidone)
BEHAVE-AD total score: 18.6 (placebo), 19.0 (risperidone)

Group 1 N= 167
Risperidone with . Mean dose 2mg - Started on 0.25 mg b.i.d. In case of insufficient response, the dosage was adjusted by increments of 0.25 mg b.i.d. No faster than every other day. Dosing was flexible throughout the treatment period according to patient response. Max dose was 2mg daily

Group 2 N= 170
Placebo with - Matching placebo
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Well covered
1.8 33% placebo, 27% risperidone
1.9 Well covered
1.10 Adequately addressed

Overall Assessment of the Study:
2.1 1-
2.2 Favours treatment
2.3 no
2.4 yes

### BULLOC2005

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n = 998</th>
<th>Age: Mean 76</th>
<th>Sex: 315 males 683 females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: Randomisation performed by an Interactive Voice Response System that automated the random assignment of treatment groups to randomisation numbers.</td>
<td>Diagnosis: 100% Alzheimer’s disease by NINCDS-ADRDA</td>
<td>Exclusions: No diagnosis of mild to moderate AD; MMSE &lt;10 or &gt;20</td>
<td></td>
</tr>
<tr>
<td>Setting: Australia, Canada, France, Germany, Italy, Spain, UK</td>
<td>Baseline: MMSE: 15.1 (SD 2.9); Donepezil 15.1 (SD 2.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Info on Screening Process: No details of screening, 998 randomised.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Data Used
- ADCS-ADL
- Global Deterioration Scale (GDS)

#### Results from this paper:

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N = 499</th>
<th>Donepezil with . Mean dose 10mg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>N = 94</td>
<td>Rivastigmine with . Mean dose 12mg/d</td>
</tr>
</tbody>
</table>

### CN 138-005

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n = 256</th>
<th>Age: Range 59-96</th>
<th>Sex: 62 males 194 females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: No details given of randomisation or allocation concealment.</td>
<td>Diagnosis: 100% Alzheimer’s disease by DSM IV</td>
<td>Exclusions: No diagnosis of AD; no psychotic symptoms of delusions or hallucinations; non-institutionalised.</td>
<td></td>
</tr>
<tr>
<td>Setting: Nursing homes or assisted living facilities. Notes: Acute phase preceded by 7-day psychotropic medication washout . Info on Screening Process: 330 enrolled in the study, 256 were randomised to the acute phase.</td>
<td>Baseline: NPI-NH Psychosis (mean): 10.75 Plb; 10.39 Aripiprazole</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Data Used
- CGI Severity of Psychosis scale
- NPI/NH

#### Type of Analysis: LOCF

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N = 128</th>
<th>Aripiprazole with - Started at 2mg/d for first week, then 5mg/d for 2 weeks, then 10mg/d for next 2 weeks and finally 15mg for remainder of acute phase.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>N = 121</td>
<td>Placebo with</td>
</tr>
</tbody>
</table>

### DEBERDT2005

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>n = 494</th>
<th>Age: Mean 79</th>
<th>Sex: 170 males 324 females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: No mention of randomisation procedure or allocation concealment.</td>
<td>Diagnosis: 81% Alzheimer’s disease by NINCDS-ADRDA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Analysis: LOCF</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Data Used
- CGI Severity of Psychosis scale
- NPI/NH

#### Group 1 | N = 204 | Olanzapine with . Mean dose 2.5mg-10mg - Half the patients assigned to olanzapine began treatment with 2.5mg/day, which was increased to 5mg/day at the end of the first week. The other half began treatment with |
**Blinding:** Double blind  
**Duration (days):** Mean 70  
**Setting:** Patients recruited from outpatient or residential settings (nursing homes or assisted living centers). 64 sites within the US.

<table>
<thead>
<tr>
<th>Group</th>
<th>N=</th>
<th>Treatment</th>
<th>Mean dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>115</td>
<td>Risperidone with</td>
<td>5mg/day.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5mg-2mg - Began with 0.5mg/day, which was increased to 1mg/day at the end of the first week.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>196</td>
<td>Placebo with</td>
<td>- Matching placebo</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>94</td>
<td>Placebo with</td>
<td>- Matching placebo</td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**

**Internal Validity:**
- 1.1 Well covered
- 1.2 Not addressed
- 1.3 Not addressed
- 1.4 Well covered
- 1.5 Well covered
- 1.6 Adequately addressed
- 1.7 Well covered
- 1.8 20% placebo, 31% risperidone, 38% olanzapine
- 1.9 Well covered
- 1.10 Not addressed

**Overall Assessment of the Study:**
- 2.1 1-
- 2.2 favours treatment
- 2.3 no
- 2.4 yes

**DEDEYN1999B**

**Study Type:** RCT (individual)  
**Study Description:** Predefined computer generated randomisation code from Janssen Research Foundation, patients no's assigned in consecutive order. Identical packaging.  
**Type of Analysis:** ITT  
**Blinding:** Double blind  
**Duration (days):** Mean 84  
**Setting:** Institutionalised patients only, 51 centers in 8 countries.  
**Notes:** Double-blind phase preceded by a 1-week single blind washout phase during which all psychotropic medications were discontinued.  
**Info on Screening Process:** 371 recruited and entered washout period, 27 discontinues in washout period, 344 were randomised.

| n= 344 | Age: Mean 81 Range 56-97  
Sex: 150 males 194 females  
Diagnosis:  
- 67% Alzheimer’s disease by DSM IV  
- 26% Vascular Dementia by DSM IV  
- 7% Mixed Dementia by DSM IV  
Exclusions: <55 years of age, not institutionalised, no diagnosis of dementia, >23 MMSE. Other conditions that diminish cognitive function; other psychiatric disorders; clinically relevant organic or neurologic disease; ECG or laboratory abnormalities; administration of a depot neuroleptic within one treatment cycle of visit 1; history of allergic reaction to neuroleptics or history of neuroleptic  
Data Used  
Cohen-Mansfield Agitation Inventory Score  
Behave-AD  
Group 1 N= 115  
Risperidone with. Mean dose 1mg - Started with 0.25mg, with increments of 0.25mg every 4 days, if indicated, to 1mg twice daily. If patients reached 1 mg twice daily without sufficient therapeutic response & no signs of EPS, dose could then be increased to a maximum of 2mg twice daily.  
Group 2 N= 115  
Haloperidol with. Mean dose 1mg - Started with 0.25mg, with increments of 0.25mg every 4 days, if indicated, to 1mg twice daily. If patients reached 1 mg twice daily without sufficient therapeutic response & no signs of EPS, dose could then be increased to a maximum of 2mg twice daily.  
Group 3 N= 114  
Placebo with - Identical matching placebo |
malignant syndrome; participation in clinical trials with investigational drugs during the 4 weeks preceding this trial.

Baseline: BEHAVE-AD total: 16.3 risperidone, 16.5 haloperidol, 16.6 placebo
CMAI total aggressive (CI): 25.6 risperidone, 26.3 haloperidol, 27.5 placebo
CGI severity (CI): 4.3 risperidone, 4.4 haloperidol, 4.4 placebo
MMSE total (CI): 8.6 risperidone, 7.9 haloperidol, 8.8 placebo

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Well covered
1.4 Well covered
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Well covered
1.8 40% risperidone, 29% haloperidol, 35% placebo
1.9 Well covered
1.10 Not addressed

Overall Assessment of the Study:
2.1 1+
2.2 unsure
2.3 no - very high drop out rate
2.4 yes

Data Used
CGI-C
NPI/NH

DEDEYN2004

Study Type: RCT (individual)
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 70
Setting: Resided in long-term nursing homes or continuing care hospitals in Europe, Australia, Israel, Lebanon and South Africa. 61 sites
Info on Screening Process: 652 randomly assigned to treatment

n = 652
Age: Mean 77
Sex: 163 males 489 females
: Diagnosis:
100% Alzheimer's disease by NINCDS-ADRDA
:
Exclusions: <40 years old; no clinically significant psychotic symptoms due to AD (delusions/hallucinations had to be moderate in severity, present at least once per week for the month preceding study entry, require pharmacological intervention); diagnosis of current primary mood disorder or other Axis 1 disorder.

Baseline: NPI/NH mean score; Olz 1.0 = 34.5, Olz 2.5 = 33.7, Olz 5.0 = 34.2, Olz 7.5 = 34.7, placebo = 32.6

Group 1 N= 129
Olanzapine with . Mean dose 1mg - Given a single 1.0mg capsule of olanzapine daily (qhs) throughout the study period.

Group 2 N= 134
Olanzapine with . Mean dose 2.5mg - Given a single 2.5mg capsule of olanzapine daily (qhs) throughout the study period.

Group 3 N= 125
Olanzapine with . Mean dose 5mg - Began therapy on 2.5mg/day for the first week and were tritrated to 5mg by 2.5mg/week increments.

Group 4 N= 132
Olanzapine with . Mean dose 7.5mg - Began therapy on 2.5mg/day for the first week and were tritrated to 7.5mg by 2.5mg/week increments.

Group 5 N= 129
Placebo with - Matching placebo

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Not addressed
1.3 Not addressed
1.4 Well covered
1.5 Adequately addressed
DEDEYN2005

Study Type: RCT (individual)
Study Description: No details given on randomisation or allocation concealment.
Type of Analysis: LOCF
Blindness: Double blind
Duration (days): Mean 70
Setting: Noninstitutionalised participants (i.e., those living in assisted living facilities or adult communities, or with a caregiver).
Notes: Randomisation preceded by a minimum 7-day washout period for previous psychotropic medication.
Info on Screening Process: Details of screening not given.

ERKINJUNTTI2002

Study Type: RCT (individual)
Study Description: Randomisation code generated by the Janssen Research Foundation (ratio two to one for galantamine vs placebo).
External allocation concealment.
Blindness: Double blind
Duration (days): Mean 180
Setting: Multi-Centred - undertaken in 10 countries
Info on Screening Process: 750 screened 158 excluded - did not meet inclusion criteria, withdrew consent, other reasons.

Data Used

**DATA USED**

**DEDEYN2005**

- **Group 1**: N=106
  - Aripiprazole with . Mean dose 2-15 mg/d - Started at 2mg/d administered once daily for 10 weeks. Could be titrated to higher doses (5, 10 and 15 mg/d) at 2 week intervals (or more rapidly based on investigator's judgement) if the patient showed insufficient clinical response.

- **Group 2**: N=102
  - Placebo with - Administered once daily

**Notes:** NPI-Psychosis primary efficacy outcome

**ERKINJUNTTI2002**

- **Group 1**: N=396
  - Galantamine with . Mean dose 24mg - Started on 4mg/day in the first week, with weekly increment of 4mg/day until they reached 24 mg/day in week 6. Administered as single tablets taken orally twice daily.

- **Group 2**: N=196
  - Placebo with - Administered as identical single tablets taken orally twice daily.
cerebral neoplasia, mental retardation or oligophrenia. Concomitant cardiovascular disease thought likely to prevent completion of the study. Concomitant epilepsy or clinically sig. psychiatric, hepatic, renal, pulmonary, metabolic or endocrine disturbances. An active peptic ulcer. History of sig. drug or alcohol abuse. Received investigational medication within the previous 30 days.

Notes: Alzheimer's disease with cerebrovascular disease
Baseline: ADAS-cog: 24.1 (placebo), 22.3 (galantamine)
MMSE: 20.2 (placebo), 20.7 (galantamine)
NPI: 11.4 (placebo), 12.2 (galantamine)

**Results from this paper:**

**Internal Validity:**
1.1 Well covered
1.2 Adequately addressed
1.3 Adequately addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 Placebo 17%, Galantamine 26%
1.9 Well covered
1.10 Not addressed

**Overall assessment of the study:**
2.1 1+
2.2 Increase the effect of Galantamine
2.3 Yes
2.4 Yes

---

**F1D-MC-HGAO**

**Study Type:** RCT (individual)

**Study Description:** Details of randomisation and allocation concealment not given.

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 56

**Followup:** 14 week open-label extension

**Setting:** 28 study centres

**Notes:** Double blind period preceded by 1 week screening and washout period. After 4 weeks of acute therapy, non responders could move to open-label extension

**Info on Screening Process:** 289 entered, 238 randomised to treatment.

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>N= 120</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI Severity of Psychosis scale</td>
<td>Olanzapine with</td>
<td>Mean dose 1-8mg/day - 1-mg tablets, once daily in the evening (from 1 to 8 tablets per day; therefore, 1 to 8mg/day dosing)</td>
</tr>
<tr>
<td>MMSE</td>
<td>Placebo with</td>
<td></td>
</tr>
<tr>
<td>Brief Psychiatric Rating Scale (BPRS)</td>
<td>- Placebo tablets, once daily in the evening.</td>
<td></td>
</tr>
<tr>
<td>Behave-AD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Data Used**

- MMSE
- CIBIC-plus

**Group 2 N= 118**

Placebo with - Placebo tablets, once daily in the evening.

---

**FELDMAN2001**

**Study Type:** RCT (individual)

**Study Description:** Randomised in a 50/50 split using a computerised randomisation schedule.

**Blindness:** Double blind

**Duration (days):** Mean 168

**Setting:** Canada, Australia, France. P's resided

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>N= 144</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>Donepezil with</td>
<td>Mean dose 10mg/day</td>
</tr>
<tr>
<td>CIBIC-plus</td>
<td>Placebo with</td>
<td></td>
</tr>
</tbody>
</table>

Group 2 N= 146

Placebo with

Concomitant medication: 11% of donepezil and 8% PLB took psychotropic medication at baseline at during trial.
either in the community or assisted living settings.

Info on Screening Process: 393 screened, 102 screen failures, 291 randomised to treatment.

Exclusions: No diagnosis of possible or probable AD; MMSE <5 or >17; FAST >6 at baseline.

Baseline: NPI: Donepezil; 19.55 (SE 1.48), PLB; 19.3 (SE 1.45)

Results from this paper:
Attrition:
Donepezil 23/144 (any reason); 12/144 (AE)
PLB 20/146 (any reason); 9/146 (AE)

HOLMES2004

Study Type: RCT (individual)
Study Description: Randomisation performed by an independent pharmacist who also provided numbered containers of identical tablets for each patient
Blindness: Double blind
Duration (days): Mean 168
Setting: UK
Notes: 12 weeks open label, 6 weeks randomised.

Info on Screening Process: 260 screened, 126 screen failures (failed NPI criteria, failed NINCDS-ADRDA criteria), 96 randomised.

Data Used
NPI

Group 1 N= 41
Donepezil with . Mean dose 10mg/d
Group 2 N= 55
Placebo with

Concomitant medication permitted during study, except other cholinesterase inhibitors.

Results from this paper:
Attrition:

Donepezil: 85% completed, 15% discontinued (2 had MMSE score drop of 2 or more; 3 due to adverse events; 1 poorly compliant with medication)
PLB: 82% completed, 18% discontinued (3 carers removed consent; 1 carer poorly compliant; 6 MMSE dropped by 2 or more)

KATZ1999C

Study Type: RCT (individual)
Study Description: Randomly assigned according to a randomisation code provided by the sponsor.
Type of Analysis: LOCF
Blindness: Double blind
Duration (days): Mean 84
Setting: Patients resided in a nursing home or chronic disease hospital. Conducted at 41 sites in the US

Info on Screening Process: 729 screened, 625 randomised to treatment. Reasons for exclusion; refusal and symptoms that were below the threshold for inclusion or those that were too severe,

Data Used
CGI-C
Cohen-Mansfield Agitation Inventory Score
Behave-AD

Group 1 N= 163
Placebo with - Identically appearing placebo given twice daily
Group 2 N= 149
Risperidone with . Mean dose 0.5mg/day - 0.5mg/day administered in divided doses (morning and bedtime) for 12 weeks.
Group 3 N= 148
Risperidone with . Mean dose 1mg/d - 1mg/day administered in divided doses (morning and bedtime) for 12 weeks. Doses were adjusted during the first double-blind week in increments of 0.5mg/day every 2 days.
Group 4 N= 165
Risperidone with . Mean dose 2mg/d - 2mg/day administered in divided doses (morning and bedtime) for 12 weeks. Doses were adjusted during the first double-blind week in increments of 0.5mg/day every 2 days.
Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Adequately addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 28% placebo, 22% 0.5mg/d, 31% 1mg/d, 41% 2mg/d
1.9 Well covered
1.10 Not addressed

Overall Assessment of the Study:
2.1 1++

MCKEITH2000C

Study Type: RCT (individual)
Study Description: Randomisation list computer generated with proprietary computer app., acc. to randomised block design. Allocation concealment - sealed envelope.

Blindness: Double blind
Duration (days): Mean 140
Follow-up: 3 weeks
Setting: Recruited from dementia assessment clinics in Spain, UK and Italy
Info on Screening Process: Not stated

Data Used
CGC-plus
MMSE
NPI

Group 1 N=59
Rivastigmine with . Mean dose 6mg - Started with 1.5mg given twice a day. Doses were escalated by 1.5mg twice daily for a maximum of 2 weeks at each dose until 6mg twice daily or a maximum well tolerated maintenance dose was reached. Titration lasted up to 8 weeks.

Group 2 N=61
Placebo with - As rivastigmine, plus, rivastigmine and placebo were presented in identical yellow capsules, size 2, and supplied in duplex blister packs containing 20 capsules for morning and evening administration over 10 days.

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Adequately addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Adequately addressed
1.8 31% rivastigmine, 16% placebo
1.9 Well covered
1.10 Not reported

Overall Assessment of the Study:
2.1 1++
2.2
2.3 Yes

Diagnosis that could have accounted for the observed psychotic disturbances.

Baseline: BEHAVE-AD: 15.9 (placebo), 15.9 (0.5mg/day), 16.0 (1mg/day), 15.4 (2mg/day)

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Well covered
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Well covered
1.8 28% placebo, 22% 0.5mg/d, 31% 1mg/d, 41% 2mg/d
1.9 Well covered
1.10 Not addressed

Overall Assessment of the Study:
2.1 1+

Data Used
CGC-plus
MMSE
NPI

n= 120
Age: Mean 74 Range 57-87
Sex: 68 males 52 females

Diagnosis:
100% Dementia with Lewy Bodies by MMSE

Exclusions: No clinical diagnosis of probable Lewy-body dementia, MMSE <9, no written informed consent, less than 5 out of 7 days per week contact with responsible caregiver, not proficient in the language in which psychometric tests were provided. Severe extrapyramidal symptoms, ie, a Hoehn and Yahr score >3 or scores >3 for rigidity, tremor or bradykinesia on the UPDRS. Asthma or known hypersensitivity to drugs closely similar to rivastigmine in structure or pharmacological action. Taking neuroleptics, anticholinergics, selegiline or similar.

Baseline: MMSE: Rivastigmine = 17.9, Placebo = 17.8
### MD-01

**Study Type:** RCT (individual)  
**Blindness:** Double blind  
**Duration (days):** Mean 168  

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 178</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memantine with</td>
<td>Mean dose 20mg/d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 172</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo with</td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**  
**Attrition:**  
Memantine 44/178  
PLB 46/172

### MD-10/PESKIND2004

**Study Type:** RCT (individual)  
**Blindness:** Double blind  
**Duration (days):** Mean 168  

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 201</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memantine with</td>
<td>Mean dose 20mg/d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 202</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo with</td>
<td></td>
</tr>
</tbody>
</table>

**Results from this paper:**  
**Attrition:**  
Memantine 36/201  
PLB 35/202

### MEEHAN2002

**Study Type:** RCT (individual)  
**Study Description:** Multi-centre, parallel-group. No details of randomisation procedure or allocation concealment.  
**Type of Analysis:** ITT  
**Blindness:** Double blind  
**Duration (days):** Mean 1  

| Setting: | Inpatients (hospitalised or nursing home patients). 33 sites in the US, 2 in Russia, 3 in Romania. |  
| Info on Screening Process: | 331 screened, 272 randomised to treatment. 59 not randomised due to criteria not being met, physician decision, patient decision, adverse events. |  

**Results from this paper:**  
**Attrition:**  
Memantine 36/201  
PLB 35/202

**Data Used**  
Agitation-Calmness Evaluation Scale (ACES)  
Cohen-Mansfield Agitation Inventory Score  
PANSS Excited Component

| n= 272 |  
| Age: | Mean 78  Range 54-97 |  
| Sex: | 106 males  166 females |  
| Diagnosis: | Alzheimer’s disease by DSM IV |  
| Vascular Dementia by DSM IV | |  
| Mixed Dementia by DSM IV | |  
| Exclusions: | <55 years of age; <14 on the Excited |  

| n= 71 |  
| Olanzapine with | Mean dose 2.5mg - Injection 1 and 2 consisted of 2.5 mg olanzapine. Injection 2, if deemed clinically necessary, was given at least 2 hours after injection 1. Injection 3 (if deemed necessary) was 1.25 mg olanzapine and was given at least 1 hour after injection 2. |  

| n= 66 |  
| Olanzapine with | Mean dose 5.0mg - Injection 1 and 2 consisted of 5 mg olanzapine. Injection 2, if deemed clinically necessary, was given at least 2 hours after injection 1. Injection 3 (if deemed necessary) was 2.5 mg olanzapine and was given at least 1 hour after injection 2. |
Component of the PANSS; no diagnosis of clinically significant agitation for which treatment with a parenteral agent is indicated; receiving benzodiazepines, antipsychotics or anticholinergics within 4h prior to first injection of study drug; received psychostimulants or reserpine within one week prior to study drug administration; diagnosis of any serious neurological condition other than AD or vascular dementia that could contribute to psychosis or dementia; laboratory or ECG abnormalities with clinical implications for the patients participation in the study; judged to be at serious risk of suicide.

Baseline: Overall means (SD):
  MMSE 11.8 (7.1)
  BPRS 35.6 (10.4)
  PANSS-EC 19.75 (13.0)
  ACES 2.18 (0.71)
  CMAI 6.97 (6)

Results from this paper:
Internal Validity:
1.1 Well covered
1.2 Not addressed
1.3 Not addressed
1.4 Well covered
1.5 Well covered
1.6 Well covered
1.7 Adequately addressed
1.8 6% olz 2.5mg, 8% olz 5mg, 10 Izp, 11% placebo
1.9 Well covered
1.10 Not addressed

Overall Assessment of the Study:
2.1 1-
2.2 favours treatment
2.3 no
2.4 yes

NUNEZ2003
N= 202
Age:
Sex: no information
Diagnosis:
  100% Alzheimer's disease
Exclusions: No diagnosis of mild to moderate possible or probable AD; MMSE <10 or >26
Baseline: MMSE: donepezil 18.8 (SD4.8), PLB 18.5 (SD 4.8)

Results from this paper:
Attrition:
Not reported.

REISBERG2003A

Group 1 N=99
Donepezil with . Mean dose 10mg/d
Group 2 N=103
Placebo with

Concomitant medication: no other interventions were reported.
**RIS-USA-232**

**Study Type:** RCT (individual)

**Study Description:** No details given on randomisation or allocation concealment.

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 56

**Setting:** Residents of a nursing home or long-term care facilities.

Notes: Acute phase was preceded by 7-day run in phase where antipsychotic medication was discontinued.

Info on Screening Process: 560 entered the study, 87 failed screening, 473 randomised to treatment.

**Type of Analysis:** ITT

**Diagnosis:**
- Age: Mean 83
- Sex: 109 males 364 females
- Diagnosis: 100% Alzheimer's disease
- Exclusions: <55 yrs of age; no diagnosis of dementia of the Alzheimer's type with or without a vascular component; <2 BEHAVE-AD psychosis subscale; MMSE <5 or >23; not deemed to be in need of treatment with atypical antipsychotic medication.

**n= 473**

**Baseline:**
- BEHAVE-AD psychosis subscale (mean, SD): 8.2 (4.85) Plb; 7.6 (4.10) Risperidone

**Results from this paper:**

Attrition:
- 29 discontinued treatment before week 28. Memantine = 13 due to Aes; PLB = 16 due to Aes

**Group 1 N= 235**
- Risperidone with - Risperidone supplied as 0.25 mg tablets and 0.50 mg tablets. Oral risperidone was given in a flexible dose regimen of 1 to 1.5 mg daily in two doses. The dose for all subjects was to be titrated to at least 1 mg daily.
- Setting: Residents of a nursing home or long-term care facilities.
- Duration (days): Mean 56
- Blindness: Double blind
- Study Type: RCT (individual)
- Study Description: No details given on randomisation or allocation concealment.
- Info on Screening Process: 560 entered the study, 87 failed screening, 473 randomised to treatment.

**Group 2 N= 238**
- Placebo with

**ROCKWOOD2001**

**Study Type:** RCT (individual)

**Study Description:** Randomised in 2:1 ratio using a computer generated code. Assignment kept in sealed, opaque envelopes.

**Blindness:** Double blind

**Duration (days):** Mean 84

**Setting:** US, Canada, GB, South Africa, Australia, NZ.

Info on Screening Process: 534 screened, 148 excluded, 386 randomised to treatment.

**Data Used**
- ADAS-Cog
- CIBIC-plus

**n= 386**

**Age:**
- Mean 75

**Sex:**
- 171 males 215 females

**Diagnosis:**
- 100% Alzheimer’s disease

**Exclusions:**
- No diagnosis of probable AD; MMSE <11 or >24; <2 on ADAS-Cog.

**Baseline:**
- NPI: Gal 9.2 (SE0.66); PLB 9.4 (SE 1.01)
- MMSE: Gal 19.7 (SE 0.24); PLB 19.6 (SE 0.32)

**Data Used**
- CIBIC-plus
- ADAS-Cog

**Group 1 N= 261**
- Galantamine with - Mean dose 24-32mg/d

**Group 2 N= 125**
- Placebo with

**Results from this paper:**

Attrition:
- 26/261 galantamine: 66 adverse events; 8 consent withdrawn; 3 non-compliance; 2 ineligible to continue; 2 lost to follow up; 5 other reasons
- 12/125 PLB: 5 adverse events; 3 consent withdrawn; 2 ineligible to continue; 2 lost to follow up.

**Concomitant medication:**
- antidepressant treatment allowed providing it had been stable for at least 2 months. Chloral hydrate was also permitted (as a sedative or hypnotic) but could not be used 24 hrs before an assessment.

**Data Used**
- ADCS-ADL
- CIBIC-plus

**Group 1 N= 126**
- Memantine with - Mean dose 20mg/d

**Group 2 N= 126**
- Placebo with
### STREET2000A

**Study Type:** RCT (individual)  
**Study Description:** Randomly allocated by the assignment of a unique kit number using a permuted block design at each investigational site. Identical tablets.  
**Type of Analysis:** Last observation carried forward  
**Blindness:** Double blind  
**Duration (days):** Mean 42  
**Setting:** Elderly nursing care facility residents. Conducted at 28 sites.  
**Info on Screening Process:** 288 registered, 206 randomised to treatment group. Exclusion/inclusion criteria not met, physician decision, protocol violations, adverse events, patient decision, sponsor decision  

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Study Medication</th>
<th>Dosage</th>
<th>Duration (days)</th>
<th>Setting</th>
<th>Blinding</th>
<th>Study Type</th>
<th>Study Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>Olanzapine</td>
<td>5mg</td>
<td>Mean 42</td>
<td>US</td>
<td>Double</td>
<td>RCT (individual)</td>
<td>Computer generated code used for randomisation.</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>Olanzapine</td>
<td>10mg</td>
<td>Mean 42</td>
<td>US</td>
<td>Double</td>
<td>RCT (individual)</td>
<td>Computer generated code used for randomisation.</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>Olanzapine</td>
<td>15mg</td>
<td>Mean 42</td>
<td>US</td>
<td>Double</td>
<td>RCT (individual)</td>
<td>Computer generated code used for randomisation.</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
<td>Placebo</td>
<td></td>
<td>Mean 42</td>
<td>US</td>
<td>Double</td>
<td>RCT (individual)</td>
<td>Computer generated code used for randomisation.</td>
</tr>
</tbody>
</table>

**Internal Validity:**  
1.1 Well covered  
1.2 Adequately addresses  
1.3 Poorly addressed  
1.4 Well covered  
1.5 Adequately addressed  
1.6 Adequately addressed  
1.7 Well covered  
1.8 23% placebo, 20% 5mg, 28% 10 mg, 34% 15mg drop out  
1.9 Well covered  
1.10 Not addressed  

**Overall Assessment of the Study:**  
2.1 1  
2.2 favours treatment  
2.3 no  
2.4 yes  

**Results from this paper:**  


### TARJOT2000

**Study Type:** RCT (individual)  
**Study Description:** Computer generated code used for randomisation.  
**Blindness:** Double blind  
**Duration (days):** Mean 147  
**Setting:** US  
**Info on Screening Process:** 1178 screened, 200 excluded, 978 randomised.  

| Group | N  | Study Medication | Dosage | Duration (days) | Diagnosis: 100% Alzheimer's disease by NINCDS-ADRDA | Exclusions: No diagnosis of probable AD, MMSE <10 or >22, ADAS-Cog <18 | Baseline: NPI: Gal 8mg 12.9 (SE 1.2); Gal 16mg 12.4 (SE 0.8); Gal 24mg 11.9 (SE 0.8); PLB 11.0 (SE 0.7) | Data Used | CIBIC-plus ADAS-Cog |
|-------|----|------------------|--------|----------------|-------------------------------------------------|---------------------------------------------------------------------|----------------------------------------------------------|-----------------|
| 1     | 140| Galantamine      | 8mg/d  | Mean 147       | 100% Alzheimer’s disease by NINCDS-ADRDA         | Exclusions: No diagnosis of probable AD, MMSE <10 or >22, ADAS-Cog <18 | Baseline: NPI: Gal 8mg 12.9 (SE 1.2); Gal 16mg 12.4 (SE 0.8); Gal 24mg 11.9 (SE 0.8); PLB 11.0 (SE 0.7) | Data Used | CIBIC-plus ADAS-Cog |
| 2     | 279| Galantamine      | 16mg/d | Mean 147       | 100% Alzheimer’s disease by NINCDS-ADRDA         | Exclusions: No diagnosis of probable AD, MMSE <10 or >22, ADAS-Cog <18 | Baseline: NPI: Gal 8mg 12.9 (SE 1.2); Gal 16mg 12.4 (SE 0.8); Gal 24mg 11.9 (SE 0.8); PLB 11.0 (SE 0.7) | Data Used | CIBIC-plus ADAS-Cog |
| 3     | 273| Galantamine      | 24mg/d | Mean 147       | 100% Alzheimer’s disease by NINCDS-ADRDA         | Exclusions: No diagnosis of probable AD, MMSE <10 or >22, ADAS-Cog <18 | Baseline: NPI: Gal 8mg 12.9 (SE 1.2); Gal 16mg 12.4 (SE 0.8); Gal 24mg 11.9 (SE 0.8); PLB 11.0 (SE 0.7) | Data Used | CIBIC-plus ADAS-Cog |
| 4     | 286| Placebo          |        | Mean 147       | 100% Alzheimer’s disease by NINCDS-ADRDA         | Exclusions: No diagnosis of probable AD, MMSE <10 or >22, ADAS-Cog <18 | Baseline: NPI: Gal 8mg 12.9 (SE 1.2); Gal 16mg 12.4 (SE 0.8); Gal 24mg 11.9 (SE 0.8); PLB 11.0 (SE 0.7) | Data Used | CIBIC-plus ADAS-Cog |

**Results from this paper:**  


### Use of Drugs for Concomitant Conditions

Use of drugs for concomitant conditions was permitted, with the exception of sedative-hypnotics and sedating cough and cold remedies, which were discontinued, if possible, 48 hrs before cognitive evaluation. Any other drugs anticholinergic were avoided.
## TARIOT2001

**Study Type:** RCT (individual)

**Study Description:** Randomised in blocks of 4 using a computerised randomisation schedule.

**Blindness:** Double blind

**Duration (days):** Mean 168

**Setting:** 27 nursing homes in the US

**Info on Screening Process:** 208 randomised to treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>N=</th>
<th>Data Used</th>
<th>Group Med</th>
<th>Concomitant medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>103</td>
<td>NPI/NH</td>
<td>Donepezil</td>
<td>Most allowed except those with sig. cholinomimetic or anticholinergic effects. Psychotropic meds were generally required to have been stabilised for 1 month prior to screening. 59% donepezil and 62% PLB took psychotropic meds.</td>
</tr>
<tr>
<td>2</td>
<td>105</td>
<td></td>
<td>Placebo</td>
<td></td>
</tr>
</tbody>
</table>

**Diagnoses:**
- Age: Mean 86  Range 64-102
- Sex: 36 males  172 females
- Diagnosis: 100% Alzheimer’s disease by NINCDS-ADRDA
- Exclusions: No diagnosis of possible or probable AD with CVD (but not VaD); MMSE <5 or >26; frequency of less than 3 times a week symptoms from NPI-NH.
- Baseline: NPI-NH: Donepezil 21.0 (SD 14.5); PLB 20.5 (SD 14.7)

## TARIOT2004C

**Study Type:** RCT (individual)

**Study Description:** Randomisation list generated and retained by Dept of Biostatics at Forest Laboratories

**Blindness:** Double blind

**Duration (days):** Mean 168

**Setting:** 37 US sites. P’s residing in the community.

**Info on Screening Process:** 589 screened, 185 excluded, 404 randomised.

<table>
<thead>
<tr>
<th>Group</th>
<th>N=</th>
<th>Data Used</th>
<th>Group Med</th>
<th>Stable doses of concomitant medication permitted inc. antidepressants, antihypertensives, anti-inflammatory, atypical antipsychotics, antiparkinsonian drugs, anticoagulants, laxatives, diuretics, sedatives, hypnotics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>202</td>
<td>CIBIC-plus ADCS-ADL</td>
<td>Memantine</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>201</td>
<td></td>
<td>Placebo</td>
<td></td>
</tr>
</tbody>
</table>

**Diagnoses:**
- Age: Mean 76
- Sex: 141 males  263 females
- Diagnosis: 100% Alzheimer’s disease by NINCDS-ADRDA
- Exclusions: No diagnosis of AD; MMSE <5 or >14
- Baseline: NPI: Mem 13.4 (SE 1.07), PLB 13.4 (SE 1.08)

## WILCOCK2003

**Study Type:** RCT (individual)

**Study Description:** Randomisation code generated by Janssen-Cilag UK Research Foundation.

**Blindness:** Double blind

**Duration (days):** Mean 365

**Setting:** 18 outpatient clinics in the UK

**Info on Screening Process:** 274 screened, 86 excluded, 188 randomised.

<table>
<thead>
<tr>
<th>Group</th>
<th>N=</th>
<th>Data Used</th>
<th>Group Med</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>88</td>
<td>ADAS-Cog ADL NPI</td>
<td>Donepezil with . Mean dose 10mg/d</td>
</tr>
<tr>
<td>2</td>
<td>94</td>
<td></td>
<td>Galantamine with . Mean dose 24mg/d</td>
</tr>
</tbody>
</table>

**Diagnoses:**
- Age: Mean 73  Range 53-88
- Sex: 85 males  103 females
- Diagnosis: 100% Alzheimer’s disease by NINCDS-ADRDA
- Exclusions: No diagnosis of probable AD; MMSE <9 or >18
- Baseline: MMSE: Gal 15.1, Donep 14.8

### Results from this paper:

**Attrition:**
- Memantine 30 discontinued - 15 due to Aes
- PLB 51 discontinued - 25 due to Aes
### Attrition:
Galantamine 78 completed 12 months of treatment, Donepezil 71 completed 12 months of treatment.

### WILKINSON2003

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 215</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil</td>
<td>Mean dose 10mg - Received donepezil 5 mg/day for 4 weeks and then single daily dose of 10mg each evening before bedtime until week 24. Blinding ensured by use of identical-appearing placebo and donepezil tablets.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 208</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil</td>
<td>Mean dose 5mg - Single daily dose of 5 mg taken each evening before bedtime.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 193</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>- Single daily dose taken each evening before bedtime. Identical-appearing tablets.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Type:</th>
<th>RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description:</td>
<td>Computer generated randomisation protocol used.</td>
</tr>
<tr>
<td>Blindness:</td>
<td>Double blind</td>
</tr>
<tr>
<td>Duration (days):</td>
<td>Mean 168</td>
</tr>
<tr>
<td>Setting:</td>
<td>Conducted at 51 sites in the US, Europe, Canada and Australia.</td>
</tr>
<tr>
<td>Info on Screening Process:</td>
<td>887 screened 271 excluded</td>
</tr>
<tr>
<td>Illness or AE, MMSE &lt;10 or &gt;26, imaging, laboratory, medications, withdrew consent, AD</td>
<td></td>
</tr>
</tbody>
</table>

| Data Used: | CIBIS, CIBIC-plus, ADAS-Cog |
| Baseline: | ADAS-cog: Placebo = 18.8, Donepezil 5mg = 20.8, Donepezil 10mg = 20.6 |
| MMSE: | Placebo = 22.2, Donepezil 5mg = 21.8, Donepezil 10mg = 21.5 |

### Results from this paper: 

**Internal Validity:**
- 1.1 Well covered
- 1.2 Well covered
- 1.3 Not addressed
- 1.4 Well covered
- 1.5 Well covered
- 1.6 Well covered
- 1.7 Well covered
- 1.8 16.6% placebo, 19.2% donepezil 5mg, 24.7% donepezil 10mg
- 1.9 Well covered
- 1.10 Not reported

**Overall assessment of the study:**
- 2.1 1+
- 2.2 Increase the effect of treatment
- 2.3 Not sure
- 2.4 Yes

### WINBLAD2001

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 142</th>
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<tbody>
<tr>
<td>Donepezil</td>
<td>Mean dose 10mg/d</td>
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<table>
<thead>
<tr>
<th>Group</th>
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<tbody>
<tr>
<td>Placebo</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Type:</th>
<th>RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description:</td>
<td>Randomisation performed using a computer generated randomisation list produced by Pfizer, Inc.</td>
</tr>
<tr>
<td>Blindness:</td>
<td>Double blind</td>
</tr>
<tr>
<td>Duration (days):</td>
<td>Mean 365</td>
</tr>
<tr>
<td>Setting:</td>
<td>Denmark, Finland, Norway, Sweden, The Netherlands</td>
</tr>
<tr>
<td>Info on Screening Process:</td>
<td>321 screened, 35</td>
</tr>
</tbody>
</table>

| Data Used: | Gottfries-Brane-Steen scale (GBS) |
| Baseline: | Alzheimer's disease by NINCDS-ADRDA |
| Exclusions: | No diagnosis of possible or probable AD, |

### Medication with major anticholinergic effects, such as high doses of neuroleptics, tricyclic antidepressants and medications for PD, were not permitted.
failures (did not meet entrance criteria, withdrew consent), 286 randomised to treatment.

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RUTHS2004</td>
<td>RCT on withdrawal of antipsychotics</td>
</tr>
<tr>
<td>SANTENS2003</td>
<td>Non RCT; open label trial</td>
</tr>
<tr>
<td>SCHARRE2002</td>
<td>Non RCT; open-label</td>
</tr>
<tr>
<td>SCHARRE2003</td>
<td>Non RCT; open-label</td>
</tr>
<tr>
<td>SCHMIDT2002</td>
<td>Non RCT; open-label</td>
</tr>
<tr>
<td>SCHMITT2004</td>
<td>Review</td>
</tr>
<tr>
<td>SCHNEIDER2003A</td>
<td>Non RCT</td>
</tr>
<tr>
<td>SELTZER2004</td>
<td>No appropriate outcome</td>
</tr>
<tr>
<td>SHIGENOBU2003</td>
<td>Non RCT</td>
</tr>
<tr>
<td>STAHL2003A</td>
<td>Non RCT</td>
</tr>
<tr>
<td>STREET1999E</td>
<td>Post-hoc sub-group analysis</td>
</tr>
<tr>
<td>SUH2004</td>
<td>No randomised placebo control group</td>
</tr>
<tr>
<td>TAI2000</td>
<td>No relevant outcome measure</td>
</tr>
<tr>
<td>VANREKUM2002</td>
<td>Discontinuation study</td>
</tr>
<tr>
<td>VERDOUX2005</td>
<td>Review</td>
</tr>
<tr>
<td>VERNY2004</td>
<td>Non RCT</td>
</tr>
<tr>
<td>WEINER2000A</td>
<td>Non RCT, open-label</td>
</tr>
<tr>
<td>WEISER2002A</td>
<td>Non RCT, open label</td>
</tr>
<tr>
<td>WILCOCK2000A</td>
<td>No relevant outcome</td>
</tr>
<tr>
<td>WILKINSON2001A</td>
<td>No relevant outcomes</td>
</tr>
</tbody>
</table>

References of Included Studies

**BALLARD2005** *(Published Data Only)*

**BLACK2003** *(Published Data Only)*

**BRODATY2003C** *(Published Data Only)*
BULLOCK2005 (Published Data Only)

CN 138-005 (Unpublished Data Only)

DEBERDT2005 (Published Data Only)

DEDEYN1999B (Published Data Only)

DEDEYN2004 (Published Data Only)

DEDEYN2005 (Published Data Only)

ERKINJUNTTI2002 (Published Data Only)


F1D-MC-HGAO (Unpublished Data Only)

FELDMAN2001 (Published Data Only)

HOLMES2004 (Published Data Only)

KATZ1999C (Published Data Only)

MCKEITH2000C (Published Data Only)

MD-01 (Unpublished Data Only)


MEEHAN2002 (Published Data Only)

NUNEZ2003

REISBERG2003A (Published Data Only)

RIS-USA-232 (Unpublished Data Only)


ROCKWOOD2001 (Published Data Only)

STREET2000A (Published Data Only)


TARIOT2000 (Published Data Only)


TARIOT2001 (Published Data Only)


TARIOT2004C (Published Data Only)

WILCOCK2003 (Published Data Only)

References of Excluded Studies

WILKINSON2003 (Published Data Only)

WINBLAD2001 (Published Data Only)

WINBLAD2003 (Published Data Only)

RUTHS2004 (Published Data Only)

SANTENS2003 (Published Data Only)

SCHARRE2002 (Published Data Only)

SCHARRE2003 (Published Data Only)

SCHMIDT2002 (Published Data Only)

SCHMIDT2004 (Published Data Only)

SCHNEIDER2003A (Published Data Only)

SCHNEIDER2003B (Published Data Only)

SHIGENOBU2003 (Published Data Only)

STAHL2003A (Published Data Only)

STREET1999E (Published Data Only)

SUH2004 (Published Data Only)


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**Characteristics of Included Studies**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **AKKERMAN2004** | n = 36  
Age: Mean 58  Range 34-85  
Sex: 5 males  33 females  
Diagnosis:  
100% Unspecified dementia  
Exclusions: CG: Current involvement in psychotherapy; MMSE <23; history of psychotic symptoms or chemical abuse or dependency; inability to read or comprehend English.  
Baseline: BAI: CBT 15.39 (SD 8.0); Control 11.59 (SD 8.12)  
HAMA: CBT 25.72 (SD 11.5); Control 27.71 (SD 9.22) | Data Used  
Hamilton Anxiety Rating Scale (HARS)  
Beck Anxiety Inventory (BAI) | Group 1  
N = 18  
CBT with - Conducted in small groups of 4-8 CGs. 9 weeks of didactic skills training and used a multidimensional model to address the physical, cognitive and behavioural components associated with CG anxiety through 2-hr weekly meeting. Also asked to practice skills |  
Group 2  
N = 17  
Waitlist with |

**Results from this paper:**

**Quality assessment:**

1.1 Well covered  
1.2 Poorly addressed  
1.3 Not addressed  
1.4 Not addressed  
1.5 Adequately addressed  
1.6 Well covered  
1.7 Well covered  
1.8
1.9 Not addressed
1.10 Not applicable

2.1 1-

No of participants: 35 (18 CBT Intervention; 17 Waitlist control)

1. Carer burden

Beck Anxiety Inventory, mean (SD):
Intervention: baseline 15.39 (8.0); week 10 (postintervention) 7.72 (5.37); week 16 (follow up for intervention group) 6.92 (5.84)
Control (waitlist): baseline 11.59 (8.12); week 10 (postintervention) 14.41 (9.08); week 20 (postintervention waitlist) 7.58 (7.61); week 26 (follow up for waitlist group) 5.36 (7.41)

Test for group difference: baseline F(1, 34)=1.94, p=.173; week 10 F(1, 34)=7.13 [significant group difference], p=.012

Hamilton Anxiety Scale, mean (SD): Intervention: baseline 25.72 (11.5); week 10 (postintervention) 14.44 (9.56); week 16 (follow up for intervention group) 13.58 (6.60)
Control (waitlist): baseline 27.71 (9.22); week 10 (postintervention) 27.24 (10.6); week 20 (postintervention waitlist) 14.83 (10.1); week 26 (follow up for waitlist group) 9.90 (6.5)

Conclusions: Intervention group demonstrated significantly reduced anxiety (measured by both self-report and clinician-administered questionnaires) compared to controls at post treatment and 6 week follow-up.
Uplifts of caregiving:

Caregiver gain, mean (SD):
Intervention: baseline, 30.9 (7.0); 30 days, 32.6 (7.1)
Control: baseline, 30.8 (6.7); 30 days, 30.9 (6.7)
Condition X Time Effect: F=5.35, p<.021, Effect size (small=.01; medium=.06; large=.14) =.02

Carers’ ability/knowledge:

Self-efficacy, mean (SD):
Intervention: baseline, 23.2 (7.9); 30 days, 25.7 (7.4)
Control: baseline, 22.7 (7.9); 30 days, 23.5 (8.1)
Condition X Time Effect: F=5.87, p<.016, Effect size (small=.01; medium=.06; large=.14) =.02

Ways of coping, mean (SD):
Intervention: baseline, 66.5 (11.1); 30 days, 67.5 (11.6)
Control: baseline, 65.3 (11.6); 30 days, 66.3 (10.5)
Condition X Time Effect: F=0.01, p<.971, Effect size (small=.01; medium=.06; large=.14) =.00

Intention to get support, mean (SD):
Intervention: baseline, 15.6 (6.2); 30 days, 17.4 (6.6)
Control: baseline, 15.7 (6.4); 30 days, 15.7 (6.9)
Condition X Time Effect: F=9.76, p<.002, Effect size (small=.01; medium=.06; large=.14) =.03

Conclusions: At 30 days the intervention group demonstrated significant improvements in depression, anxiety, level and frequency of stress, caregiver strain, self-efficacy, and intention to seek help, as well as perceptions of positive aspects of caregiving.

30-day follow-up tests revealed significant group X time effects (univariate repeated measures analyses of variance for each of the dependent measures) showing gains for the intervention group in seven of the eight measures, with small-to-moderate effect sizes. Compared with the control group, treatment participants reported significantly greater gains with respect to the measures of self-efficacy, intention to get support, and caregiver gain. In addition, the treatment participants reported significantly greater reductions in caregiver stress, caregiver strain, depressive symptomatology, and state anxiety compared with the control participants. The only scale that did not differ with respect to pretest-posttest change between groups was the Ways of Coping scale (measure of self-reported frequency of employing specific stress-reduction strategies).

The intervention and control groups differed significantly on caregiver stress at baseline, but controlling for baseline level the two groups differed significantly on caregiver stress at posttest (analysis of covariance, F (1, 289)=9.87, p=.002).

Internal Validity:
1.1 Well covered
1.2 Not reported
1.3 Not addressed
1.4 Poorly addressed
1.5 Poorly addressed
1.6 Poorly addressed
1.7 Well covered
1.8 3% overall
1.9 Poorly addressed
1.10 Not addressed

Overall Assessment of the Study:
2.1 -
### BURGIO2003

**Study Type:** RCT (individual)  
**Study Description:** Two-group comparison design with random assignment.  
**Type of Analysis:** ITT  
**Blindness:** Open  
**Duration (days):** Followup: 18 months  
**Setting:** In-home treatment sessions. Caregivers lived with and provided care for a relative with AD or related disorders for an average of 4 hours a day  
**Info on Screening Process:** 289 caregiver-care recipient dyads screened; 203 deemed eligible; 140 consented to participate  
**n= 118**  
- **Age:** Mean 63  
- **Sex:** 26 males 92 females  
- **Diagnosis:** 100% Unspecified dementia  
- **Exclusions:** CGs: Not white or african-american; <21 yrs of age; provided < 4 hrs of care per day; been providing care for < 6 months; involved in another psychosocial intervention; had an acute illness that would prevent them from participating for at least 6 months  
- **CRs:** no diagnosis of AD or related disorder; MMSE>24; did not exhibit at least one limitation in basic ADLs; did not display at least 3 problem behaviors identified by primary CG  
  Baseline: CR MMSE (mean, SD): 13.70 (6.82) control group; 12.51 (8.12) intervention group  
**Results from this paper:**  
**Quality assessment:**  
1. **Internal validity:**  
   - 1.1 Well covered  
   - 1.2 Well covered  
   - 1.3 Well covered  
   - 1.4 Well covered  
   - 1.5 Poorly addressed - but taken into account  
**Overall assessment of the study:**  
2. **1++**  
**Data Used**  
- **Revised Memory and Behaviour Problem Checklist**  
- **Notes:** RMBPC used to assess CR problem behaviours and CG appraisal of problem behaviours. CG social support and activity also assessed.  
**Group 1 N=61**  
- **Skills training with:** initial 3 hour workshop, 4 weekly home visits during the first month, two more visits during second month. Over next 10 months, home visits were alternated monthly with therapeutic phone calls. CGs received info on behaviour management techniques etc.  
**Group 2 N=57**  
- **Minimal support with:** Telephone support composed of empathic statements, active listening, and generic written materials.  
**Data for outcome measures shown by group assignment and race:**  
**RMBPC behav. bother (mean, SD):**  
- **Minimal Support Condition:** 1.50 (0.88) baseline control (White)  
  1.15 (0.83) 6 months control (White)  
  1.73 (1.18) baseline control (African-American)  
  1.77 (1.14) 6 months control (African-American)
Overall, there were decreasing levels of problem behaviors and appraisals of behavioral bother, and increased satisfaction with leisure activities in both groups. But possible differential responses to interventions by race and relationship to care recipient.

Conclusions: CR problem behaviours - no significant effects of treatment group  
CG appraisal - no significant effects of treatment group  
Social network, social support and activity - no significant effects of treatment group.

**COON2003**

<table>
<thead>
<tr>
<th>Group</th>
<th>N=41</th>
<th>Anger management class with - Early sessions presented Cog-Behavioural model and treatment rationale, discussed sources of caregiver frustration, taught basic relaxation skills. Then taught specific cog skills; how to generate positive self-talk, monitor unhelpful thoughts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>N=45</td>
<td>Depression management class with - Based on social learning theory, followed cog-behavioural principals in its structure. Greater emphasis placed on behavioural components - increase life satisfaction, taught relationship b/n mood and pleasant events, develop self-monitoring techniques.</td>
</tr>
<tr>
<td>Group 3</td>
<td>N=44</td>
<td>Waitlist with - Initial assessment then brief phonecalls to maintain caregivers’ interest in the study and maximise retention.</td>
</tr>
</tbody>
</table>

Interventions: 2hr workshops for 8 weeks, followed by 2 booster or skill reinforcement sessions at 1 month intervals. Format was highly structured; brief ‘check-in’, review of homework, 20 to 30 minute didactic lecture on a particular skill, homework set.

**Data Used**

- Ways of Coping Checklist-Revised (WCCL-R)
- State-Trait Anger Expression Inventory (STAXI)
- Multiple Affect Adjective Checklist (MAACL)

**Results from this paper:**

**Quality assessment:**

- Internal validity:
  - 1.1 Well covered
  - 1.2 Poorly addressed
  - 1.3 Not addressed
  - 1.4 Not addressed
  - 1.5 Adequately addressed
  - 1.6 Well covered
  - 1.7 Adequately addressed
  - 1.8 23%
  - 1.9 Poorly addressed
  - 1.10 Not applicable

- No of participants: 169 (53 Anger Management; 64 Depression Management; 52 Waitlist control)

**Carer burden**
### State Anger (STAXI), mean (SD):
- Anger Management intervention: before 13.0 (.84); after 12.1 (.75); mean change from baseline -0.9
- Depression Management intervention: before 11.7 (.76); after 11.7 (.76); mean change from baseline -2
- Wait List: before 11.5 (.84); after 13.3 (.75); mean change from baseline 1.8

### MAACL Hostility subscale, mean (SD):
- Anger Management: before 9.2 (.85); after 7.1 (.94); mean change from baseline -2.1
- Depression Management: before 11.0 (.88); after 8.0 (.97); mean change from baseline -3.0
- Wait List: before 8.5 (.85); after 10.0 (.94); mean change from baseline 1.5

### Negative coping (WCCL-R), mean (SD):
- Anger Management: before 28.1 (2.0); after 28.9 (2.1); mean change from baseline 0.8
- Depression Management: before 33.0 (2.0); after 30.0 (2.1); mean change from baseline -3.0
- Wait List: before 29.1 (1.9); after 27.9 (2.0); mean change from baseline -1.2

### MAACL Depression subscale, mean (SD):
- Anger Management: before 16.4 (1.3); after 15.0 (1.3); mean change from baseline -1.4
- Depression Management: before 17.8 (1.4); after 15.4 (1.3); mean change from baseline -2.4
- Wait List: before 14.6 (1.3); after 16.5 (1.3); mean change from baseline 1.9

### Positive coping (WCCL-R), mean (SD):
- Anger Management: before 51.1 (1.9); after 56.0 (1.8); mean change from baseline 3.9
- Depression Management: before 55.0 (1.9); after 54.4 (1.8); mean change from baseline -0.6
- Wait List: before 54.1 (1.8); after 53.6 (1.7); mean change from baseline -0.5

### Managing behaviours, mean (SD):
- Anger Management: before 57.3 (3.6); after 70.0 (3.3); mean change from baseline +12.7
- Depression Management: before 55.5 (3.6); after 59.8 (3.3); mean change from baseline +4.3
- Wait List: before 62.5 (3.6); after 60.8 (3.3); mean change from baseline -1.7

### Controlling thoughts, mean (SD):
- Anger Management: before 59.6 (3.8); after 67.3 (3.7); mean change from baseline +7.7
- Depression Management: before 52.5 (3.7); after 59.7 (3.6); mean change from baseline +7.2
- Wait List: before 68.8 (3.8); after 64.0 (3.7); mean change from baseline -4.8

### Conclusions:
Significant main effects in the expected direction found for changes in most measures.

---

### Data Used
- Geriatric Depression Scale
- Screen for Caregiver Burden (SCB)

### Group 1 N= 24
- In-home skills training with - 12 weekly skills training sessions carried out in the home focusing on: general problem solving; CG appraisal of behaviour problems; programmes for managing specific problems; strategies for handling affective responses to difficult caregiving situations.

### Group 2 N= 23
- Telephone skills training with - 12 weekly skills training sessions carried out on the phone focusing on: general problem solving; appraisal of behaviour problems; programmes for managing specific problems; strategies for handling affective responses to difficult caregiving situations.
### Results from this paper:

**Quality assessment:**

**Internal validity:**
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Adequately addressed
1.8 38%
1.9 Not addressed
1.10 Not applicable

2.1 No of participants: 44 (18 In home training; 10 Telephone training; 16 Friendly calls)

### 1. Carer burden

**Caregiving burden (SCB-A), mean (SD):**
- **In home training:** Baseline, 39.8 (12.0); T2 30.0 (10.9); T3, 31.7 (12.0)
- **Telephone training:** Baseline, 26.9 (9.8); T2 29.9 (7.8); T3, 27.4 (7.2)
- **Friendly calls:** Baseline, 37.0 (12.1); T2 35.0 (12.0); T3, 37.0 (11.8)

**Caregiving distress (SCB-B), mean (SD):**
- **In home training:** Baseline, 21.4 (13.5); T2 15.2 (9.6); T3, 12.8 (9.5)
- **Telephone training:** Baseline, 14.2 (6.6); T2 12.8 (6.3); T3, 11.2 (8.3)
- **Friendly calls:** Baseline, 18.2 (10.6); T2 15.6 (12.0); T3, 20.5 (16.3)

### Conclusions:

In-home training reduced caregiving burden and distress. Telephone training took longer to reduce burden and distress.

No significant difference between groups or between times for each group for caregiver depression, perceived social support and life satisfaction.

---

**DONE2001**

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>Study Description: Weighted block randomisation used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: No mention</td>
<td>Duration (days):</td>
</tr>
<tr>
<td>Followup: 1 week</td>
<td>Setting: Carers were visited individually, either at home or at a designated day centre. UK</td>
</tr>
<tr>
<td>Info on Screening Process: Following provisional screening, 53 suitable carers were identified and contacted, 45 were then randomised to treatment.</td>
<td>n= 45</td>
</tr>
<tr>
<td>Age:</td>
<td>Sex: no information</td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
</tr>
<tr>
<td>100% Unspecified dementia</td>
<td></td>
</tr>
<tr>
<td>Exclusions: No medical diagnosis of progressive dementia; care not informal or taking place out of the home; no form of verbal communication taking place in the relationship.</td>
<td>Baseline: AACS (mean, 95% CI): 1.7 (0.7 to 2.7) workshop group, 1.8 (0.6 to 3.0) booklet only group</td>
</tr>
<tr>
<td>Relatives stress scale score (mean, 95% CI): 30.0 (26 to 33.9) workshop group, 31.9 (28.2 to 35.6) booklet only group</td>
<td>Data Used</td>
</tr>
<tr>
<td>Thomas Assessment of Communication Inadequacy</td>
<td>Carer Stress</td>
</tr>
<tr>
<td>Assessment of Awareness about Communication Strate</td>
<td>Notes: Outcome 1 - AACS - developed specifically for this study. P’s shown scenes depicting communication breakdown and asked to write brief descriptions of what happened. Three speech and language therapists assess the descriptions for levels of awareness.</td>
</tr>
</tbody>
</table>

### Group 1 N= 30

Communication training workshop with - 2 sessions of one hour each, separate by one week. Specialist language and speech therapist presented video scenes of communication breakdowns, this was followed by group discussion on possible causes and then given successful communication strategies.

### Group 2 N= 15

Booklet control with - Given a booklet and informed it contained useful advice that they would find relevant. Booklet depicts scenes of communication breakdown and gives advice on how to deal more effectively with each problem,
Internal validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Poorly addressed
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Adequately addressed
1.8 Not addressed
1.9 Not applicable
1.10 Not addressed

2.1 1-

No of participants: 45 (30 Workshop; 15 Booklet only)

Carer burden:

Relatives stress scale score, mean (95% CI): Workshop group: Pre-intervention, 30.0 (26.0-33.9); follow up, 29.7 (25.7 to 33.7)
Booklet only group: Pre-intervention, 31.9 (28.2-35.6); follow up, 31.9 (28.0 to 35.8)
No difference in stress between the groups.

Carers' ability/knowledge:

Assessment of Awareness about Coping Strategies Test, mean (95% CI):
Workshop group: Pre-intervention, 1.7 (0.7-2.7); follow up, 1.8 (1.8 to 5.0)
Booklet only group: Pre-intervention, 1.8 (0.6-3.0); follow up, 3.4 (1.8 to 5.0)
Workshop group improved more than booklet only group: F1,43=8.6 (p=.005)

Conclusions: Training workshop group demonstrated a significantly greater awareness of communication strategies than the booklet-only group at 6 week follow-up. Both groups reported some reduction in the frequency of communication problems at home, and a reduction in the associated level of distress.

DUCHARME2005A

Study Type: RCT (individual)
Study Description: No details of randomisation.
Blindness: Single blind
Duration (days): Mean 70
Setting: Living in a residential centre. Canada.
Info on Screening Process: No details of screening. 137 randomised to treatment.

n=137
Age: Mean 54
Sex: all females
Diagnosis:
100% Unspecified dementia
Exclusions: Not the daughter or spouse or had primary responsibility for the care-recipient; living in the residential centre for less than 6 months; no diagnosis of irreversible dementia; caregivers receiving help from support group or involved in psychotherapy.

Data Used
Carers’ Assessment of Managing Index (CAMI)
Stress Appraisal Measure (SAM)
Psychological Distress Index

Group 1 N=45
Psychoeducative programme with - 10 90-min weekly sessions: How to feel at ease with the pwd; how to express your point of view to health and social care staff; how to avoid emotional torment; how to deal with small daily losses; how to identify and call upon support.
Group 2 N=51
Control with - Subjected to no programme
Group 3 N=41
Comparison with - Programme of equal duration developed independently by a Quebec Alzheimer Society and offered by its personnel.

Results from this paper:
Quality assessment:
Conclusions: At end of programme, successful outcomes in competence in dealing with health care staff and perceived challenge of the caregiver role were unique to the intervention group. Statistical support also provided for the efficacy of both the intervention and a second comparison intervention with respect to perceived threat and role overload, control by self, informal/formal social support, and use of the coping strategy of reframing.

At 3 months follow-up successful outcomes unique to the intervention group persist (competence in dealing with health care staff and perceived challenge of the caregiver role). Both the intervention and a second comparison intervention have persistent effects on perceived availability of informal and formal support.

No of participants: 137 (45 psychoeducation intervention; 51 alternative intervention; 41 control group)

Findings presented as prediction analysis.

**EISDORFER2003**

**Study Type:** RCT (individual)  
**Study Description:** Randomisation was stratified according to ethnicity of caregiver. No other details given.  
**Blindness:** No mention  
**Duration (days):** Mean 365  
**Followup:** 18 months  
**Setting:** Home-visits, Miami, USA.  
**Info on Screening Process:** No details on how many screened. 225 randomised to treatment.

<table>
<thead>
<tr>
<th>No</th>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Group 1 N= 75</td>
<td>Structural Ecosystems Therapy (SET) with - 12 months: Weekly sessions for 4 months, biweekly for 2 months, monthly for 6 months. Each session 60-90 mins. Aim to identify &amp; restructure specific interactions within family and other systems linked to CG burden. Identify problems &amp; available resources</td>
</tr>
<tr>
<td>2</td>
<td>Group 2 N= 77</td>
<td>SET + Computer-Telephone Integrated System with - Some sessions conducted by computer-telephone system, only in final 6 months of treatment. Designed to augment therapy by facilitating links btw the caregivers and their family and external supportive resources.</td>
</tr>
<tr>
<td>3</td>
<td>Group 3 N= 73</td>
<td>Minimal support with - Biweekly calls for 6 months, monthly calls for last 6 months, consisting of active listening and empathic comments. Generic educational materials were provided. Main aim to provide contact and prevent dropout.</td>
</tr>
</tbody>
</table>

| Study Type | RCT (individual)  
|------------|------------------|
| Duration (days) | Mean 365  
| Setting | Home-visits, Miami, USA.  
| Info on Screening Process | No details on how many screened. 225 randomised to treatment.

**Data Used**  
Revised Memory and Behaviour Problem Checklist  
Center for Epidemiological Studies Depression scale

**Group 1** N= 75  
Structural Ecosystems Therapy (SET) with - 12 months: Weekly sessions for 4 months, biweekly for 2 months, monthly for 6 months. Each session 60-90 mins. Aim to identify & restructure specific interactions within family and other systems linked to CG burden. Identify problems & available resources

**Group 2** N= 77  
SET + Computer-Telephone Integrated System with - Some sessions conducted by computer-telephone system, only in final 6 months of treatment. Designed to augment therapy by facilitating links btw the caregivers and their family and external supportive resources.

**Group 3** N= 73  
Minimal support with - Biweekly calls for 6 months, monthly calls for last 6 months, consisting of active listening and empathic comments. Generic educational materials were provided. Main aim to provide contact and prevent dropout.

**Results from this paper:**

| Quality assessment |  
|--------------------|------------------|
| **Internal validity:** |  
| 1.1 Well covered |  
| 1.2 Poorly addressed |  
| 1.3 Not addressed |  
| 1.4 Not addressed |  
| 1.5 Adequately addressed |  
| 1.6 Well covered |  
| 1.7 Well covered |  
| 1.8 After 6 months: 42 % control, 28% SET, 34% SET+CTIS |  
| 1.9 Adequately addressed |  
| 1.10 Not applicable |  
| 2.1 1- |  

**No of participants:** 225
Data for outcome measures shown by group assignment and race (changes over 18 months; minimal support n=41, family therapy n=54, family therapy + technology n=59):

**Carer depression:**

Cuban American - CES-D, mean (SD):
- Minimal Support control: baseline, 17.70 (8.9); 6 months 18.60 (8.3)
- Family therapy intervention: baseline, 21.77 (14.3); 6 months, 18.81 (12.3)
- Family therapy + technology intervention: baseline, 19.31 (9.3); 6 months, 14.41 (8.9)

White non-Hispanic - CES-D, mean (SD):
- Minimal Support control: baseline, 18.60 (8.3); 6 months 13.28 (7.4)
- Family therapy intervention: baseline, 14.91 (10.7); 6 months, 14.91 (10.7)
- Family therapy + technology intervention: baseline, 15.67 (11.8); 6 months, 13.87 (8.8)

**Conclusions:**

Caregivers in combined family therapy (Structural Ecosystems Therapy) and technology (Computer Telephone Integrated System) intervention experienced a significant reduction in depressive symptoms. At 6 months and 18 months, the family therapy + technology intervention was effective in decreasing caregiver depression (varying according to ethnicity and relationship to care recipient). In general, family therapy only was not effective in lowering caregiver outcomes.

---

**FLATLEY1995**

Study Type: RCT (individual)  
Study Description: No details on randomisation provided  
Blindness: No mention  
Duration (days):  
Followup: 12 months  
Setting: In-home, US.  
Info on Screening Process: No screening details provided.

<table>
<thead>
<tr>
<th>n= 102</th>
<th>Age: Mean 64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: 34 males 68 females</td>
<td></td>
</tr>
</tbody>
</table>

**Diagnosis:**
- 100% Alzheimer's disease

**Exclusions:**
- Did not have primary responsibility for a person with AD living at home; did not have a local telephone exchange; unable to read and write English.

**Data Used**
- Decision making confidence and skill
- IESS (Instrumental and Expressive Social Support)
- Impact of Caregiving Scale (Burden)
- Center for Epidemiological Studies Depression scale

**Results from this paper:**

Quality assessment:

- Internal validity:
  1.1 Well covered
  1.2 Poorly addressed
  1.3 Not addressed
  1.4 Not addressed
  1.5 Adequately addressed
  1.6 Well covered
  1.7 Adequately addressed
  1.8 8% ComputerLink, 4% control.
  1.9 Not addressed
  1.10 Not applicable

- No of participants: 102 (51 control; 51 experimental)

**Carer burden:**

Physical impact of caring, mean (SD):
- Control: baseline 10.5 (3.49); 12 months 11.6 (3.9)
- Experimental: baseline 10.8 (3.3); 12 months 11.4 (4.0)

Relational impact of caring, mean (SD):
Control: baseline 12.0 (3.4); 12 months 11.5 (3.3)
Experimental: baseline 12.2 (3.54); 12 months 12.1 (3.9)

Emotional impact of caring, mean (SD):
Control: baseline 11.6 (2.0); 12 months 10.9 (2.5)
Experimental: baseline 11.4 (3.2); 12 months 11.0 (3.4)

Social impact of caring, mean (SD):
Control: baseline 14.0 (2.3); 12 months 12.9 (2.7)
Experimental: baseline 13.7 (2.1); 12 months 12.8 (3.2)

Carer depression:
Control, mean (SD): baseline 15.6 (10.6); 12 months 15.7 (10.5)
Experimental, mean (SD): baseline 21.2 (8.1); 12 months 18.9 (11.0)

Carers' ability/knowledge:
Decision-making skills, mean (SD):
Control: baseline 2.51 (.91); 12 months 2.37 (.78)
Experimental: baseline 2.53 (.78); 12 months 2.4 (.61)
F(1, 95) = 1.69, p<.20

Decision making confidence, mean (SD):
Control: baseline 54.65 (7.3); 12 months 54.7 (6.1)
Experimental: baseline 51.9 (6.0); 12 months 56.8 (7.0)
F(1, 95) = 9.73, p<.01

Conclusions: The computer network intervention group experienced greater improvement in confidence in decision-making but no significant improvement in decision-making skill or decreased perceived social isolation.

FUNG2002

Study Type: RCT (individual)
Study Description: No details of randomisation.
Blindness: No mention
Duration (days): Mean 84
Setting: Recruited from 2 large centres that provided day care and caregiving resources, Hong Kong
Info on Screening Process: No details of how many were screened. The centres provided care to 400 clients. 60 randomised, 8 withdrew, leaving 26 p's in each condition.

Results from this paper:

Quality assessment:

1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Well covered
1.8 13.3% of each condition

Data Used
Use of mental health services
WHOQOL-BREF(HK)
NPI-Caregiver Distress Scale
Notes: WHOQOL-BREF(HK): World Health Organisation Quality of Life Measure-Brief Version

Group 1 N= 26
Mutual Support Programme with - 12 weekly 1 hr sessions. Consisted of education, sharing & discussion, psychological support, problem solving, emotional effect of caregiving, improvement of interpersonal relationships, establishing support outside the group, improving home care skills

Group 2 N= 26
Conventional Family Service with - Services included: medical consultation and advice about dementia, advice and referrals on financial aids and welfare services, educational talks in dementia care, social and recreational activities arranged by the centre

Age: 18-30 = 13, 31-50 = 16, 51-70 = 14, 71-82 = 9
No of participants: 52 (26 control; 26 experimental)

Carer burden:

NPI-D total score, mean (SD): Experimental group: pretest 47.20 (10.11); posttest 36.80 (9.38); Control group: pretest 47.87 (12.68); posttest 42.49 (13.56)

F=5.099, p=0.003

Carer wellbeing:

WHOQOL-BREF(HK) total score, mean (SD): Experimental group: pretest 96.90 (14.11); posttest 113.21 (9.98); Control group: pretest 103.75 (0.68); posttest 88.19 (9.56)

F=23.145, p=0.000

Conclusions: Significant differences in distress levels and in quality of life with greater improvements in the mutual support group.

Data Used
65-item Profile of Mood States (POMS)

Group 1 N=
PLST with - Progressively Lowered Stress Threshold model: Two 3 hr home visits. First focused on developing therapeutic relationship while teaching underlying principles of the model (planning care strategies/discussing troublesome behaviour) Second...

Group 2 N=
Comparison with - Identical to experimental group with the exception of education based on the PLST model

PLST intervention: Second home care visit, care plan reviewed and specific behavioural techniques taught. Supporting literature left with carer. Continued with telephone contact every other week for 6 months, reinforcing PLST intervention and plan.

Results from this paper:

Quality assessment:

Internal validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Adequately addressed
1.5 Poorly addressed, but differences taken into account
1.6 Well covered
1.7 Adequately addressed
1.8
1.9 Not addressed
1.10 Not applicable

2.1 1-

No of participants: 37

Carer burden:

Total mood disturbance, mean (SD): Experimental: Baseline, 36.67 (35.59); 1 week, 36.24 (31.39); 6 months, 29.80 (38.58)
Comparison: Baseline, 57.14 (25.07); 1 week, 58.14 (30.82); 6 months, 39.79 (36.77)
Group by time interaction effect, Group main effect and Time main effect all not significant.

Conclusions: Significant effects of intervention on T-cell immune function, but no significant effects on mood disturbance and natural killer cell cytotoxicity.

Effect size for treatment group assignment on Total Mood Disturbance scores was $R^2=0.050$, indicating a very weak association between treatment group status and mood-outcomes.

GERDNER2002

Study Type: RCT (individual)
Study Description: No details of how p's were randomised.
Blindness: No mention
Duration (days):
Followup: 12 months
Setting: In home visits. P's recruited at 8 research sites in Iowa, Minnesota, Indiana, Arizona.
Info on Screening Process: No details on how many screened. 241 recruited, 237 usable for analysis.

Data Used
Memory and Behavior Problems Checklist

Group 1 N= 132
PLST with - 4 hours of in-home intervention. Received individualised plan applying PLST model, typically included structured routine with regular rest periods. Taught to modify environment, encouraged to develop activities to promote past interests.

Group 2 N= 105
Comparison with - 2 one hour visits two weeks apart. Recived routine information, referrals for community based services, case management and support groups. Received relevant books and brochures.

Results from this paper:
Quality assessment:
Internal validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Adequately addressed
1.8 2%
1.9 Adequately addressed
1.10 Not applicable

2.1 -

Carers' ability/knowledge:

Caregiver response to behavioural problems: There was a trend toward reduction of reactions over time for the experimental group, indicated by negative effect (-0.39, $p<0.01$) on the time effect for the intervention variable.


Care recipients' symptoms:

Frequency of behavioural problems: Effect varies by relationship. Significant increase in non-spouse comparison group, no significant difference in time trend between spouse caregiver experimental and comparison groups.

Conclusions: Statistically significant ($p<0.01$) beneficial effects of intervention on response to memory and behavioural problems for all carers and on response to ADL problems for spouse carers only. Reduced reporting of the frequency of memory and behavioural problems by nonspouse carers in the intervention group.

GITLIN2003A

Study Type: RCT (individual)
Study Description: Randomised using permuted blocks and prepared by site statistician. Concealed using opaque sealed envelopes.

Data Used
Task Management Strategy Index
Caregiving Mastery Index
Revised Memory and Behaviour Problem Checklist

Group 1 N= 89
Environmental Skill Building Programme with - ESP - provide caregivers with education about disease process and impact of environments on behaviour, problem-solving techniques, technical skills to modify the home. Five 90-min home visits and one 30-min telephone
Blindness: No mention
Duration (days):
Followup: 12 months
Setting: Home visits and telephone contact in Philadelphia, US. Recruited from Philadelphia Corporation for Aging and media announcements.

Info on Screening Process: 413 screened, 290 eligible, 255 willing to participate, 188 participated in 6-month follow up.

Exclusions: CGs: <21 yrs of age; provided < 4 hrs of care per day; been providing care for < 6 months; involved in another psychosocial intervention; had an acute illness that would prevent them from participating for at least 6 months
CRs: no diagnosis of AD or related disorder; MMSE>24; did not exhibit at least one limitation in basic ADLs; did not display at least 3 problem behaviors identified by primary CG

Baseline: Care recipients had mean MMSE score of 12.08 (SD=7.21)

Results from this paper:
Quality assessment:

Internal validity:
1.1 Well covered
1.2 Well covered
1.3 Well covered
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Adequately addressed
1.8 26%
1.9 Not addressed
1.10 Not applicable

2.1 1+

No of participants: 190 (89 Experimental; 101 Comparison)

1. Carer burden

Objective burden
Total days receiving ADL help, mean:
Experimental: Baseline 2.6; 6-months 2.19
Usual Care: Baseline 2.26; 6-months 2.51
p=.026 (95% CI .66, .97)

Subjective burden
RMBPC upset with memory related behaviours, mean (SD):
Experimental: Baseline 0.81 (0.86); 6-months 0.65 (0.75)
Usual Care: Baseline 0.72 (0.77); 6-months 0.78 (0.85)
p=.027 (95% CI -.35, -.02)

3. Carer wellbeing

Perceived change in affect, mean (SD):
Experimental: Baseline 2.86 (0.72); 6-months 3.09 (0.62)
Usual Care: Baseline 2.97 (0.62); 6-months 2.91 (0.66)
p=.034 (95% CI .01, .36)

At 1 year follow-up (65 Experimental; 65 Comparison) intervention caregivers showed significantly greater improvement in affect that control caregiver (difference in adjusted means 0.24, p=.033). There was also a trend for maintenance of skills and reduced behavioural occurrences but no gains in other outcome measures.

Conclusions: At 6 months the Environmental Skill-Building Programme reduced (objective and subjective) burden and enhanced caregiver well-being in select domains and has added benefit for women and spouses.

Compared with controls, intervention caregivers reported less upset with memory-related behaviours, less need for assistance from others and better affect.

HEBERT2003
Results from this paper:

Significant effect of support group program

No of participants: 118 (60 psychoeducation intervention; 58 control group)

1. Carer burden

RMBPC reaction, mean change from baseline (SD): Study Group, -0.28 (.55); Control Group, -0.10 (.60); p=0.04
RMBPC cross-product, mean change from baseline (SD): Study Group, -0.61 (1.53); Control Group, 0.13 (1.86); p=0.02
RMBPC disruptive behaviours reaction, mean change from baseline (SD): Study Group, -0.41 (.87); Control Group, -0.03 (.83); p<0.01
RMBPC disruptive behaviours cross-product, mean change from baseline (SD): Study Group, -0.51 (1.86); Control Group, 0.20 (1.64); p=0.03
Zarit Burden Interview, mean change from baseline (SD): Study Group, -2.40 (14.96); Control Group, 0.09 (11.99); p= .39
State-Trait Anxiety Inventory, mean change from baseline (SD): Study Group, -1.27 (16.47); Control Group, -1.64 (14.49); p=0.39
Psychiatric Symptoms Index, mean change from baseline (SD): Study Group, -1.16 (7.98); Control Group, 0.65 (6.03); p=0.13

3. Carer wellbeing

Bradburn Affective Scale (higher score for more positive affect), mean change from baseline (SD): study group, 0.08 (3.39); control -0.19 (3.02); p=0.49

5. Carers' ability/knowledge

Personal efficacy scale (higher score for better perceived efficacy), mean change from baseline (SD): study group, -3.08 (20.71); control 0.06 (21.73); p=0.74

6. Care recipients' symptoms

RMBPC frequency, mean change from baseline (SD): study group, -0.07 (.41); control 0.12 (.51); p=0.06
RMBPC disruptive behaviours frequency, mean change from baseline (SD): study group, -0.06 (.56); control 0.15 (.61); p=0.08

RMBPC = Revised Memory and Behaviour Problem Checklist

Conclusions: Quality assessment:

Internal validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Not addressed
1.4 Poorly addressed
### HUANG2003

**Study Type:** RCT (individual)

**Study Description:** Each given registration number, odd's assigned experimental group, even's control.

- **Blindness:** Single blind
- **Duration (days):** Mean 90
- **Setting:** Home visits. Northern Taiwan.

**Info on Screening Process:** 110 screened, 75 eligible, 59 agreed to participate and were randomised. Final sample of 48.

**Diagnosis:**
- **Age:** Mean 56  Range 28-80
- **Sex:** 13 males  35 females
- **Exclusions:** CR: no diagnosis of dementia; <65 yrs of age; score <50 on CMAI.

**Results from this paper:**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N= 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skills training with - 2 session (each separated by a week) in home training programme (based on PLST model), telephone consultations every 2 weeks. Aim to identify behavioural problems and plan a schedule to minimize/handle them.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2</th>
<th>N= 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control with - Received written education materials and social telephone follow-ups every two weeks.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Cohen-Mansfield Agitation Inventory Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n= 48</td>
</tr>
<tr>
<td></td>
<td>Age: Mean 56  Range 28-80</td>
</tr>
<tr>
<td></td>
<td>Sex: 13 males  35 females</td>
</tr>
<tr>
<td></td>
<td>Diagnosis: 100% Unspecified dementia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: CR: no diagnosis of dementia; &lt;65 yrs of age; score &lt;50 on CMAI.</td>
</tr>
</tbody>
</table>

### Quality assessment:

<table>
<thead>
<tr>
<th>Internal validity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1  Well covered</td>
</tr>
<tr>
<td>1.2  Poorly addressed</td>
</tr>
<tr>
<td>1.3  Not addressed</td>
</tr>
<tr>
<td>1.4  Poorly addressed</td>
</tr>
<tr>
<td>1.5  Adequately addressed</td>
</tr>
<tr>
<td>1.6  Well covered</td>
</tr>
<tr>
<td>1.7  Well covered</td>
</tr>
<tr>
<td>1.8  20% experimental, 17% control</td>
</tr>
<tr>
<td>1.9  Poorly addressed</td>
</tr>
<tr>
<td>1.10 Not applicable</td>
</tr>
</tbody>
</table>

**No of participants:** 48 (24 Experimental; 24 Comparison)

### 5. Carers’ ability/knowledge

Self efficacy of caregivers for management of behavioural problems (CMAI)*, mean (SD):

- **Experimental:** pretest 138.83 (22.08); 3 weeks 153.33 (14.25); 3 months 164.75 (11.02)
- **Change from pretest to 3 weeks:** p<.001
- **Change from 3 weeks to 3 months after training programme:** p<.001
- **Control:** pretest 134.50 (17.72); 3 weeks 133.46 (17.78); 3 months 135.50 (17.14)
- **Change from pretest to 3 weeks:** p=.889
- **Change from 3 weeks to 3 months after training programme:** p<.016

[*Results for 4 subscales also given.*]

### 6. Care recipients’ symptoms

CMAI*, mean (SD) [p-value: change from pretest to 3 weeks, change from 3 weeks to 3 months after training programme]:

- **Experimental:** pretest 88.79 (34.31); 3 weeks 81.25 (35.62); 3 months 75.88 (34.75)
- **Change from pretest to 3 weeks:** p<.001
- **Change from 3 weeks to 3 months after training programme:** p<.001
- **Control:** pretest 80.08 (22.58); 3 weeks 82.33 (23.21); 3 months 82.0 (22.97)
**MAHONEY2003**

<table>
<thead>
<tr>
<th>Study Type:</th>
<th>RCT (individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description:</td>
<td>Computer generated random assignment lists generated for each recruitment site.</td>
</tr>
<tr>
<td>Type of Analysis:</td>
<td>ITT</td>
</tr>
<tr>
<td>Info on Screening Process:</td>
<td>143 selected from recruitment, 118 met eligibility criteria, 100 enrolled.</td>
</tr>
</tbody>
</table>

### Data Used

- **State Anxiety Inventory (STAI)**
- **Center for Epidemiological Studies Depression scale**
- **Revised Memory and Behaviour Problem Checklist**

### Group 1 N=49

Technology intervention with - Access to Interactive Voice Response system for 12 months. System provided caregiver stress monitoring and counselling information, personal voicemail linkage to AD experts, voicemail telephone support group, distraction call for care recipients.

### Group 2 N=51

Usual Care Control with - Given reference booklet, containing similar information to the intervention, that provided strategies to manage AD-related disruptive behaviours.

### Results from this paper:

#### Quality assessment:

1.1 Well covered
1.2 Well covered
1.3 Not addressed
1.4 Poorly addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Well covered
1.8
1.9 Well covered
1.10 Not applicable

2.1 RMBPC bothersome behaviours, mean (SD):

- **Technology**:
  - baseline 14.9 (14.4); 6 months 11.5 (9.4); 12 months 14.1 (11.9); 18 months 12.2 (11.0)
  - Control: baseline 11.1 (10.3); 6 months 12.8 (11.2); 12 months 10.3 (11.1); 18 months 12.3 (13.1)

- **CES-D depressive symptoms, mean (SD):**

  - **Technology**: baseline 13.7 (11.1); 6 months 12.3 (9.1); 12 months 12.4 (11.5); 18 months 12.0 (10.3)
  - **Control**: baseline 13.5 (11.0); 6 months 14.9 (11.7); 12 months 13.6 (12.0); 18 months 14.5 (11.7)

- **STAI anxious symptoms, mean (SD):**

  - **Technology**: baseline 20.9 (6.8); 6 months 19.8 (5.7); 12 months 20.2 (6.8); 18 months 19.0 (6.5)
  - **Control**: baseline 20.9 (6.6); 6 months 20.6 (7.7); 12 months 20.7 (7.5); 18 months 20.7 (7.6)

#### Conclusions:

Overall, no main effect of the intervention in reducing bother scores, depression or state anxiety.

Spouses that exhibited low mastery and high anxiety benefited the most from the intervention. Suggestion that interventions should be tailored to match users' characteristics.
### MARTINCOOK2003

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>Study Description: No details of randomisation given.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: No mention</td>
<td>Duration (days): Mean 28</td>
</tr>
<tr>
<td>Followup: 14 weeks</td>
<td>Setting: Texas, US.</td>
</tr>
<tr>
<td>Info on Screening Process: No details given on screening. 37 caregivers randomised to treatment.</td>
<td></td>
</tr>
<tr>
<td>n= 37</td>
<td>Age:</td>
</tr>
<tr>
<td></td>
<td>Sex: no information</td>
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<tr>
<td></td>
<td>Diagnosis:</td>
</tr>
<tr>
<td></td>
<td>100% Unspecified dementia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: Not the primary caregiver of a person with dementia.</td>
</tr>
<tr>
<td>Data Used</td>
<td>NPI</td>
</tr>
<tr>
<td></td>
<td>Steinmetz Control Scale</td>
</tr>
<tr>
<td></td>
<td>Caregiver Resentment</td>
</tr>
<tr>
<td>Group 1 N= 19</td>
<td>Psychoeducative programme with - Four weekly 2-hr sessions.</td>
</tr>
<tr>
<td></td>
<td>1. Overview of AD, symptoms, course, treatments</td>
</tr>
<tr>
<td></td>
<td>2. Learning and implementing management strategies</td>
</tr>
<tr>
<td></td>
<td>3. Environmental and safety issues</td>
</tr>
<tr>
<td></td>
<td>4. Emphasised common caregiver feelings and coping skills.</td>
</tr>
<tr>
<td>Group 2 N= 18</td>
<td>Waitlist with - Put on a waiting list for attendance in the psychoeducational group.</td>
</tr>
</tbody>
</table>

#### Results from this paper:

**Quality assessment:**

- Internal validity:
  - Well covered
  - Poorly addressed
  - Not addressed
  - Adequately addressed
  - Well covered
  - Poorly addressed
  - Not addressed
  - Adequately addressed
  - Well covered
  - Adequately addressed
  - Not addressed
  - Not applicable

- Results presented as correlations.

- Conclusions: No significant effects of intervention on carers’ resentment or depression.

### MARTINCOOK2005

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>Study Description: No details of randomisation given.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: No mention</td>
<td>Duration (days): Mean 28</td>
</tr>
<tr>
<td>Followup: 17 weeks</td>
<td>Setting: Community or retirement and assisted living services, Texas, US.</td>
</tr>
<tr>
<td>Info on Screening Process: 49 recruited, 47 enrolled and randomised to treatment.</td>
<td></td>
</tr>
<tr>
<td>n= 47</td>
<td>Age:</td>
</tr>
<tr>
<td></td>
<td>Sex: 14 males 33 females</td>
</tr>
<tr>
<td></td>
<td>Diagnosis:</td>
</tr>
<tr>
<td></td>
<td>100% Unspecified dementia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: No diagnosis of dementia according to established clinical criteria; not community dwelling; not mild to moderate; no consistent caregiver; unstable usage of psychotropic medications.</td>
</tr>
<tr>
<td>Baseline: Care-recipient MMSE: intervention 19 (SD 7.5), control 19.8 (SD 6.6)</td>
<td></td>
</tr>
<tr>
<td>Data Used</td>
<td>Global Deterioration Scale (GDS)</td>
</tr>
<tr>
<td></td>
<td>NPI</td>
</tr>
<tr>
<td></td>
<td>ADCS-ADL</td>
</tr>
<tr>
<td></td>
<td>Independent Living Scale</td>
</tr>
<tr>
<td>Group 1 N= 24</td>
<td>Skills training with - Using the Texas Functional Living Scale (TFLS) as an eductional tool, over 4 weekly sessions CGs were taught supportive skills, especially with regard to enhancing ADLs.</td>
</tr>
<tr>
<td></td>
<td>Control with</td>
</tr>
<tr>
<td>Group 2 N= 23</td>
<td></td>
</tr>
</tbody>
</table>

#### Results from this paper:

**Quality assessment:**

- Internal validity:
  - Well covered
  - Poorly addressed
  - Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Adequately addressed
1.8 5%
1.9 Not addressed
1.10 Not applicable

2.1

Independent Living Scale:

Intervention group: 1.48 (SE 2.75) week 1; -0.38 (SE 2.87) week 7; 0.57 (SE 2.87) week 17
Control group: 5.96 (SE 2.63) week 1; 2.25 (SE 2.69) week 7; 6.17 (SE 2.69) week 17

NPI:

Intervention group: 12.48 (SE 2.58) week 1; 11.95 (SE 2.64) week 7; 10.41 (SE 2.64) week 17
Control group: 13.56 (SE 2.48) week 1; 12.58 (SE 2.53) week 7; 10.63 (SE 2.53) week 17

ADCS-ADL-MCI

Intervention group: 31.65 (SE 3.26) week 1; 31.05 (SE 3.33) week 7; 30.64 (SE 3.33) week 17
Control group: 35.20 (SE 3.12) week 1; 39.08 (SE 3.19) week 7; 36.21 (SE 3.19) week 17

GDS:

Intervention group: 3.00 (SE 0.47) week 1; 2.09 (SE 0.48) week 7; 2.68 (SE 0.48) week 17
Control group: 1.76 (SE 0.45) week 1; 1.67 (SE 0.46) week 7; 1.58 (SE 0.46) week 17

Conclusions: The expected relationship between depression and caregiver sense of self-efficacy was found.

Carer depression:

No significant effect of intervention on geriatric depression scale.

Uplifts of caregiving:

No significant difference (group, time and group by time interactions) in the finding meaning through caregiving provisional meaning scale (ability to find positive meaning through caregiving).

Carers' ability/knowledge:

No significant effect of intervention on the general self efficacy scale
No significant effect of intervention on the finding meaning through caregiving
Loss/Powerlessness scale (measure of carers' feeling of empowerment).

Care recipients' symptoms:

No significant difference (group, time and group by time interactions) in neuropsychiatric inventory.

MITTELMAN2004A

<table>
<thead>
<tr>
<th>Study Type: RCT (individual)</th>
<th>No mention</th>
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<tbody>
<tr>
<td>Study Description: Randomised by lottery.</td>
<td>No mention</td>
</tr>
<tr>
<td>Blindness: No mention</td>
<td>No mention</td>
</tr>
<tr>
<td>Duration (days):</td>
<td>No mention</td>
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<tr>
<td>Followup: 4 years</td>
<td>No mention</td>
</tr>
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<td>Setting: Living at home, New York, US.</td>
<td>No mention</td>
</tr>
<tr>
<td>Info on Screening Process: No details given,</td>
<td>No mention</td>
</tr>
</tbody>
</table>

n = 406
Age: Mean 71
Sex: 162 males 244 females

Diagnosis:
100% Alzheimer’s disease

Exclusions: Not the spouse of someone with a clinical

Data Used
Global Deterioration Scale (GDS)
Memory and Behavior Problems Checklist

Group 1 N= 203
Multicomponent intervention with - First 4 months; structured intervention given in same format but content derived from needs of CG, e.g. techniques for managing troublesome behaviours, promoting communication. Then joined support groups that met weekly. Also ad-hoc counselling by phone.
406 randomised to treatment.

Diagnosis of AD; didn’t have primary responsibility; not living at home; did not have at least one other relative living in New York.

Baseline: MBPC frequency: treatment 41.2 (SD 18.3); control 46.7 (SD 19.4)

Results from this paper:

Quality assessment:
Internal validity:
1.1 Well covered
1.2 Adequately addressed
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Well covered
1.8 9%
1.9 Not addressed
1.10 Not applicable

2.1 1-

No of participants at baseline: 406 (203 treatment, 203 control).

Carer burden:

Main effect for treatment group (p=.0226) indicates that carers receiving the intervention report lower reaction (bother) scores on average than control carers across all assessments after baseline (4 months to 4 years).

Group X time interaction effect (p=.0368) indicates that the group difference became stronger with length of follow-up.

Pairwise comparisons of the covariate-adjusted predicted scores indicate that the treatment carers had significantly lower appraisals of bother than the control carers beginning at 1-year follow-up (p=.037) and continuing to 4 year follow-up (p-values < .02).

Carer depression:

Difference in change of Geriatric Depression Scale score between treatment and usual care groups significant at 1-year follow-up showing a benefit for the treatment group according to intent to treat analysis:

Treatment group, mean (SD): -1.1 (5.0)
Usual care group, mean (SD): 0.3 (6.0)
F=6.40, df=1, 404, p=.02

Magnitude of difference between groups decreased with time, but after controlling for baseline variables, carers in the treatment group had significantly lower depression scores than control group carers through 3.1 years after enrollment (p<.05).

Care recipients’ symptoms:

The frequency of behaviour problems increases over time for both groups, with virtually no difference between the groups in the pattern of change over the 4 year follow-up.

Conclusions: Reduced caregivers’ reaction (bother) ratings in the intervention group - group differences are statistically significant and increase over time after controlling for baseline differences.
Baseline: MMSE: treatment group 14.9 (SD 8.63); control group 15.2 (SD 8.57)

Results from this paper:

Quality assessment:

Internal validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Well covered
1.8 33%
1.9 Not addressed
1.10 Not addressed
2.1 -

Zarit Burden Interview, mean (SD):
Treatment group: 14.3 (7.09) baseline; 14.1 (8.07) 12 months; 13.7 (8.2) 18 months; 13.8 (8.2) 24 months; 13.7 (8.49) 36 months
Control group: 14.3 (7.17) baseline; 14.9 (8.17) 6 months; 14.4 (8.62) 12 months; 14.3 (8.62) 18 months; 14.2 (8.6) 24 months; 14.2 (8.73) 36 months

Geriatric Depression Scale, mean (SD):
Treatment group: 4.24 (3.29) baseline; 4.28 (3.40) 12 months; 4.17 (3.55) 18 months; 4.06 (3.51) 24 months; 4.2 (3.52) 36 months
Control group: 4.21 (3.28) baseline; 4.42 (3.68) 12 months; 4.53 (3.8) 18 months; 4.36 (3.65) 24 months; 4.49 (3.61) 36 months

Conclusions: Statistically significant, but very small reductions in caregiver burden and depression:

Nobili2004

Study Type: RCT (individual)
Study Description: Randomisation table used.
Type of Analysis: LOCF secondary analysis completed.
Blindness: No mention
Duration (days):
Followup: 12 months
Setting: Home visits. Italy.
Info on Screening Process: No details of screening. CG's contacting Federazione Alzheimer Italia were assessed for eligibility.

n=69
Age: Mean 56
Sex: 13 males 56 females

Diagnosis:
100% Unspecified dementia

Exclusions: CR; no clinical diagnosis of dementia; score <2 on problem behaviours; have no problem behaviours; live outside the home; live outside 10 miles of Milan; didn't have a principle carer.

Baseline: RSS (Relative's stress scale) total score (0-60) mean, SD: 28.3 (11.3) control, 31.5 (10.5) experimental.

Data Used
Relative's Stress Scale
Spontaneous Behaviour Interview (SBI-C)

Group 1 N=35
Structured intervention with - 2 home visits: 1) psychologist 60 mins: discuss CG stress and consequences, verbal and non verbal communication, how to manage problem behaviour. 2) occupational therapist 90 mins: practical advice on preventing/managing problem behaviour, home env etc

Group 2 N=34
Control with - Provided with free help line, information about the rights of patients and families, legal aspects, how to file forms for the economical help by the State, and addresses of community services and specialised clinical centres.

Results from this paper:

Quality assessment:

Internal validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Not addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Well covered
1.8 37% intervention group, 31% control group
<table>
<thead>
<tr>
<th>Study Type: Systematic Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness:</td>
</tr>
<tr>
<td>Duration (days):</td>
</tr>
</tbody>
</table>

Results from this paper:
Quality assessment:
Internal validity:
1.1 Well covered
1.2 Well covered - good inclusion/exclusion criteria
1.3 Poorly addressed
1.4 Well covered
1.5 Poorly addressed - but taken into account
Overall assessment of the study:
2.1 1+

STOLLEY2002

Study Type: RCT (individual)
Study Description: No details of randomisation provided.
Blindness: Single blind
Duration (days):
Followup: 12 months
Setting: Iowa and Minnesota, US.
Info on Screening Process: No details of screening. 247 enrolled, data reported for 241 as 6 dropped out before being assigned to a group.

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N= 133</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoeducative programme with - 4 hrs of in-home intervention; CG given individualised plan of care based on the PLST model. At 2nd visit, plan was reviewed, techniques were taught and written materials summarizing the plan were provided.</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>N= 108</td>
</tr>
<tr>
<td>Control with - 2 hr visits twice a week at two-week intervals for a total of four hours of intervention. General information about dementia and legal, care and safety issues were presented.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data Used</th>
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</thead>
<tbody>
<tr>
<td>Philadelphia Geriatric Center Caregiving Appraisal</td>
</tr>
<tr>
<td>Memory and Behavior Problems Checklist</td>
</tr>
</tbody>
</table>

n= 241
Age: Mean 65  Range 35-87
Sex: 62 males  179 females

Diagnosis:
66% Alzheimer’s disease
5% Multi-infarct dementia
6% Mixed Dementia

No of participants: 69 (35 Experimental; 34 Comparison)

Carer burden:
Caregiver stress - no significant difference between control and intervention groups in caregiver stress (RSS scores).
Care recipients’ symptoms:
The reduction in the SBI-C score (index of frequency of problem behaviours) between baseline and 12 month follow-up was significantly greater in the intervention group than the control group (-3.6 ± 4.1 vs. -0.9 ± 3.3; p=0.03).
Conclusions: At 12 months, the frequency of problem behaviours was significantly more reduced in the intervention group. No significant differences seen between the control group and intervention group in terms of patients’ cognitive and functional changes, or time spent caring and caregivers’ RSS (stress) scores, although there was a nonsignificant reduction in caregiver stress in the intervention group.
Results from this paper:

Quality assessment:

Internal validity:
1.1 Well covered
1.2 Poorly addressed
1.3 Not addressed
1.4 Poorly addressed
1.5 Adequately addressed
1.6 Well covered
1.7 Adequately addressed
1.8
1.9 Not addressed
1.10 Not applicable

2.1 1-

No of participants: 241 (133 Experimental; 108 Comparison)

Details of data not given

Carer burden:
Statistically significant effect of intervention indicating less negative impact (p=.029)
Statistically significant group differences in perception of burden (p=0.26)

Uplifts of caregiving:
Positive statistically significant effect of intervention on perceived satisfaction (p=.006) after initial fall for intervention group.

Carers’ ability/knowledge:
No difference in mastery scores between groups over time

Care recipients’ symptoms:
Intervention effects not reported.

Conclusions: The intervention was influential in increasing positive appraisal and decreasing negative appraisal of the caregiving situation, with statistically significant beneficial effects on impact, burden, and satisfaction, but no intervention effect on mastery.
Results from this paper:
No of participants: Intervention, baseline 47; Posttest (2 Month) 42; 6 Months 32; Control, baseline 48; Posttest (2 Month) 41; 6 Months 34

Carer burden:

SCB-Subjective Burden, Mean (SD):
Control: Baseline, 23.4 (12.2); Posttest (2 Month), 23.1 (14.1); Change at Posttest, 0.3 (7.6); 6 Month 25.8 (13.7)
Intervention: Baseline, 24.7 (12.4); Posttest (2 Month), 20.1 (10.6); Change at Posttest, -4.4 (7.7); 6 Month 21.4 (12.5)
Pre-Post p=.011, Longitudinal p=.029

RMBPC-Caregiver Reaction, Mean (SD):
Control: Baseline, 25.0 (14.7); Posttest (2 Month), 23.3 (16.0); Change at Posttest, -1.6 (7.6); 6 Month 23.4 (14.5)
Intervention: Baseline, 28.1 (15.9); Posttest (2 Month), 22.3 (15.8); Change at Posttest, -5.8 (9.8); 6 Month 21.9 (15.6)
Pre-Post p=.024, Longitudinal p=.037

Caregiver Sleep Questionnaire, Mean (SD):
Control: Baseline, 10.5 (3.9); Posttest (2 Month), 10.1 (4.2); Change at Posttest, -0.4 (2.5); 6 Month 9.1 (5.2)
Intervention: Baseline, 11.3 (3.9); Posttest (2 Month), 9.9 (3.6); Change at Posttest, -1.4 (3.2); 6 Month 9.2 (4.6)
Pre-Post p=.124, Longitudinal p=.033

Carer depression:

CES-D, Mean (SD):
Control: Baseline, 13.2 (8.5); Posttest (2 Month), 13.6 (9.3); Change at Posttest, 0.6 (6.3); 6 Month 15.8 (10.5)
Intervention: Baseline, 14.8 (9.1); Posttest (2 Month), 12.4 (7.6); Change at Posttest, -2.1 (6.4); 6 Month 12.5 (7.7)
Pre-Post p=.046, Longitudinal p=.023

Hamilton Depression Scale, Mean (SD):
Control: Baseline, 7.6 (5.0); Posttest (2 Month), 7.8 (5.3); Change at Posttest, 0.2 (3.2); 6 Month 8.5 (5.7)
Intervention: Baseline, 6.9 (4.1); Posttest (2 Month), 6.3 (4.5); Change at Posttest, -0.6 (3.9); 6 Month 6.7 (3.9)
Pre-Post p=.284, Longitudinal p=.041

Care recipients’ symptoms:

RMBPC-Memory Subscale, Mean (SD):
Control: Baseline, 3.0 (0.8); Posttest (2 Month), 3.0 (0.9); Change at Posttest, 0.0 (0.7); 6 Month 3.1 (1.0)
Intervention: Baseline, 3.0 (0.7); Posttest (2 Month), 2.8 (0.8); Change at Posttest, -0.2 (0.6); 6 Month 2.8 (0.8)
Pre-Post p=.070, Longitudinal p=.031

Quality of Life - Alzheimer’s Disease proxy report, Mean (SD):
Control: Baseline, 28.3 (4.9); Posttest (2 Month), 28.4 (4.9); Change at Posttest, 0.1 (3.8); 6 Month 28.2 (4.6)
Intervention: Baseline, 27.8 (5.5); Posttest (2 Month), 29.4 (5.2); Change at Posttest, 1.6 (3.6); 6 Month 28.4 (5.4)
Pre-Post p=.049, Longitudinal p=.031

Longitudinal analysis uses data for 2 and 6 months, controlled for baseline values (last values carried forward for missing data).

Conclusions: At 2 months intervention caregivers had significantly (p<.05) greater reductions in self-reported depression, subjective burden, and reactions to behavior problems than caregivers in the routine medical care group (intention to treat analysis). Intervention caregivers also reported that, compared with controls, their family members with Alzheimer’s disease had significantly greater quality of life.

At 6 months follow-up, intervention caregivers continued to have significantly (p<.05) greater reductions in caregiver depression (CES-D difference, mean = -2.3, 95% CI= -0.6 to 0.0), subjective burden (mean difference= -4.2, 95% CI= -7.6 to 0), and reactivity to dementia-related behaviors (mean difference= -3.2, 95% CI= -6.1 to -0.2). At 6 months intervention caregivers also had significant decreases in depression
on the HDRS (mean difference = -1.2, 95% CI = -2.4 to -0.0), significant reductions in self-reported sleep problems (mean difference = -1.1, 95% CI = -2.2 to -0.1) and reported fewer memory-related problem behaviors (mean difference = -0.3, 95% CI = -0.5 to -0.0). Intervention caregivers continued to report significantly greater quality of life for their family members with Alzheimer’s disease compared with controls.

**Internal Validity:**
1.1 Well covered
1.2 Not reported
1.3 Not addressed
1.4 Poorly addressed
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Well covered
1.8 Not addressed
1.9 Poorly addressed
1.10 Adequately addressed

**Overall Assessment of the Study:**
2.1 -

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**WOODS2003**

**Study Type:** Non-randomised controlled trial

**Blindness:** Open

**Duration (days):**

**Followup:** 8 months

**Setting:** London, UK. 76% of sample lived at home.

**Info on Screening Process:** 128 recruited and interviewed at baseline, 104 interviewed at follow-up.

**Gender and age shown are that of the carer**

**Data Used**
- Quality of relationship
- Clinical Dementia Rating Scale
- General Health Questionnaire (GHQ)

**Group 1 N = 43**
- Admiral Nursing Service with - Provided information, and practical and emotional support to carers. Focus on the carer as a client and continue to provide support after the pwd has entered residential care or died.

**Group 2 N = 61**
- Comparison with - Referral to conventional services, usually see work with the caregiver as secondary to that with the patient.

**Results from this paper:**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHQ Total, mean (SD)</td>
<td>20.2 (9.4) Admiral Nurse; 19.4 (8.9) comparison</td>
<td></td>
</tr>
<tr>
<td>GHQ Somatic, mean (SD)</td>
<td>5.4 (3.2) Admiral Nurse; 5.0 (3.7) comparison</td>
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<tr>
<td>GHQ Anxiety, mean (SD)</td>
<td>5.1 (3.3) Admiral Nurse; 6.0 (4.0) comparison</td>
<td></td>
</tr>
<tr>
<td>GHQ Social, mean (SD)</td>
<td>7.5 (2.3) Admiral Nurse; 7.3 (2.1) comparison</td>
<td></td>
</tr>
<tr>
<td>GHQ Depression, mean (SD)</td>
<td>2.2 (3.3) Admiral Nurse; 1.3 (2.2) comparison</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Statistically significant reduction in carer anxiety/insomnia.

**Internal Validity:**
1.1 Well covered
1.2 Not reported
1.3 Not reported
1.4 Not reported
1.5 Adequately addressed
1.6 Adequately addressed
1.7 Adequately addressed
1.8 Not reported
1.9 Not addressed
1.10 Not addressed

**Overall Assessment of the Study:**
2.1 -

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**WRIGHT2001**

**Study Type:** RCT (individual)

**Study Description:** Block sampling technique used for randomisation.

**Data Used**
- Center for Epidemiological Studies Depression scal
- Carer Stress

**Group 1 N = 68**
- Structured intervention with - Home visit 1-2 weeks, 5-6 weeks & 12 weeks after discharge. Phonecalls at 6 & 12 months. Intervention: strategies for handling People with dementia with disruptive behaviours were stabilized in an inpatient setting. Behavioural Intensive Care Unit (BICU)
Characteristics of Excluded Studies

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUCHANAN2004</td>
<td>Exclude as dissertation abstract and no paper identified in Pub Med or Google.</td>
</tr>
<tr>
<td>BURNS2003</td>
<td>Exclude as does not meet inclusion criteria - comparison is between 2 interventions.</td>
</tr>
<tr>
<td>GALLAGHERTHOMPS2003</td>
<td>Exclude as does not meet inclusion criteria - comparison is between 2 interventions (psychoeducational vs. support groups)</td>
</tr>
<tr>
<td>GITLIN2003</td>
<td>Meta-analysis of 5 REACH studies</td>
</tr>
<tr>
<td>GOODMAN1990A</td>
<td>Exclude as study compares two interventions (Sorenson inclusion criteria not met)</td>
</tr>
<tr>
<td>JABLONSKI2005</td>
<td>Does not appear to be applicable to the Sorenson carer interventions.</td>
</tr>
<tr>
<td>JANG2004</td>
<td>Post-hoc analysis of previous trial</td>
</tr>
<tr>
<td>JARROTT2005</td>
<td>Does not appear to be applicable to the Sorenson carer interventions.</td>
</tr>
<tr>
<td>KUZU2005</td>
<td>Exclude as before after comparison of intervention effect with no control group.</td>
</tr>
<tr>
<td>LAVOIE2005</td>
<td>Exclude as only qualitative findings presented.</td>
</tr>
<tr>
<td>RIVIERE2001</td>
<td>non-randomised</td>
</tr>
</tbody>
</table>

References of Included Studies

AKKERMAN2004  
MAHONEY2003 (Published Data Only)

MARTINCOOK2003 (Published Data Only)

MARTINCOOK2005 (Published Data Only)

MITTELMAN2004A (Published Data Only)

NEWCOMER1999 (Published Data Only)

NOBILI2004 (Published Data Only)

SORENSEN2002 (Published Data Only)

STOLLEY2002 (Published Data Only)

TERI2005A (Published Data Only)

WOODS2003 (Published Data Only)

WRIGHT2001 (Published Data Only)

References of Excluded Studies

BUCHANAN2004 (Unpublished Data Only)

BURNS2003 (Published Data Only)

GALLAGHERTHOMPS2003 (Published Data Only)


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