BEST in Mental Health

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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

"For people with mild and moderate dementia, how effective is group cognitive stimulation therapy compared to any other intervention, in improving cognition, communication and quality of life?"

Clarification of question using PICO structure

Patients:	Adults with mild and moderate dementia
Intervention:	Group cognitive stimulation therapy
Comparator:	Any other intervention
Outcome:	Improving cognition, communication and quality of life

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Clinical and research implications

There is some evidence, from one methodologically flawed systematic review and two additional, very small randomised controlled trials, that cognitive stimulation therapy (CST) may be effective in improving cognition, communication and quality of life in people with mild to moderate dementia. However, there is no substantive evidence to support the longer term effectiveness of CST, beyond the end of treatment.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified one systematic reviews1 and three additional randomised controlled trials (RCTs)[3,4,5] that included data relevant to this evidence summary. One further RCT was excluded because it evaluated cognitive stimulation therapy (CST) as part of a combined intervention.[2] All of the included studies assessed the effectiveness of CST compared to control/placebo. The systematic review reported data for multiple outcomes (cognition, self-reported quality of life and well-being, communication and social interaction, mood, activities of daily living, and behaviour) post-intervention and, where available, at follow-up.1 Two additional RCTs reported data on post-treatment measures of cognitive function, but did not include measures of communication or quality of life, or follow-up data.[3,4] The final RCT considered the effectiveness of maintenance CST, following an initial 7 week programme and reported data on cognition and quality of life at 3 and 6 months follow-up.[5]

Main Findings

The systematic review found evidence to support the short-term (post-treatment) effectiveness CST for improving cognition (SMD 0.41 (95% CI: 0.25 to 0.57), 14 studies) and staff ratings of communication and social interaction (SMD 0.44 (95% CI: 0.17 to 0.71), 4 studies), and some evidence that CST may be effective in improving quality of life post-treatment (SMD 0.38 (95% CI: 0.11 to 0.65), 4 studies).[1] Data from two studies included in this review indicated that there were no significant effects of CST on cognition, communication , or quality of life, at ten months follow-up.[1] Two additional, very small RCTs both reported significantly better Mini Mental State Examination (MMSE) scores in the CST group than in the control group, at the end of treatment;[3,4] neither of these studies reported any follow-up data. The third RCT, which assessed the effectiveness of maintenance CST, found no significant effects on cognition or participant-reported quality of life at six months follow-up.[5] However, proxy quality of life measures (reported by family or care givers) suggested that maintenance CST was associated with improved quality of life compared to treatment as usual: mean difference proxy QoL-AD = 1.53 (95% CI: 0.37 to 2.69), p=0.01; mean difference proxy DEMQOL = 3.24 (95% CI: 0.29 to 6.19), p=0.03.[5]

Authors Conclusions

One systematic review concluded that cognitive stimulation interventions benefit cognition in people with mild to moderate dementia and that possible effects on self-reported quality of life and well-being require further exploration. Two additional RCTs reported that CST was associated with improved cognition in people with mild to moderate dementia and one further RCT concluded that continuing CST improves quality of life and improves cognition for those taking acetylcholinesterase inhibitors.

Reliability of conclusions/Strength of evidence

The systematic review included in this evidence summary had significant methodological weaknesses. In particular, identification of relevant studies was inadequate, and the meta-analyses were of questionable validity. The two additional RCTs that assessed a CST as a primary intervention were both very small and included only short-term outcome data; the reporting of the methods was weak for both of these trials. The RCT that assessed the effectiveness of maintenance CST was of generally good methodological quality.

What do guidelines say?

NICE guidelines for supporting people with dementia (CG42, 2006) make the following recommendations for the use of cognitive stimulation therapy;

"People with mild-to-moderate dementia of all types should be given the opportunity to participate in a structured group cognitive stimulation programme. This should be commissioned and provided by a range of health and social care staff with appropriate training and supervision, and offered irrespective of any drug prescribed for the treatment of cognitive symptoms of dementia." (pp. 26)

SIGN guidelines for the management of patient with dementia (CG86, 2006) make the following comments and recommendations regarding cognitive stimulation in dementia treatment;

"Cognitive stimulation may occur informally through recreational activities, or formally through:

- a programme of memory provoking, problem-solving and conversational fluency activities
- the spaced retrieval method
- face name training.

Formal cognitive stimulation produced a positive clinical impact on cognitive function in people with dementia. Although memory of specific pieces of information was improved it did not produce general benefits to memory function. These studies did not generalise to overall neuropsychological function and had short follow up.

Cognitive stimulation should be offered to individuals with dementia.

Cognitive stimulation training can be carried out at home by a caregiver, with no risk to the person with dementia and with minimal training/education of the carer." (pp. 8)

The findings of this evidence summary are consistent with current guidelines.

Date question received: 12/09/2014
Date searches conducted: 15/09/2014
Date answer completed: 20/10/2014

References

Systematic reviews

1. Woods, B., Aguirre, E., Spector, A.E. and Orrell, M. (2012) Cognitive stimulation to improve cognitive functioning in people with dementia. *Cochrane Database of Systematic Reviews.*

Randomised controlled trials

2. Maci, T., Le Pira, F., Quattrocchi, G., Di Nuovo, S., Perciavalle, V., & Zappia, M. (2012). Physical and Cognitive Stimulation in Alzheimer Disease. The GAIA Project A Pilot Study. *American Journal of Alzheimer's Disease and Other Dementias*, *27*(2), 107-113. - **EXCLUDED – This study assessed a combined intervention, comprising cognitive stimulation, physical activity, and socialisation and does not provide any information on the effectiveness of CST (any effects observed could be due to any or all of the components of the intervention).**
3. Mapelli, D., Di Rosa, E., Nocita, R., & Sava, D. (2013). Cognitive stimulation in patients with dementia: randomized controlled trial. *Dementia and Geriatric Cognitive Disorders Extra*, *3*(1), 263-271.
4. Niu, Y. X., Tan, J. P., Guan, J. Q., Zhang, Z. Q., & Wang, L. N. (2010). Cognitive stimulation therapy in the treatment of neuropsychiatric symptoms in Alzheimer's disease: a randomized controlled trial. *Clinical Rehabilitation, 24*(12), 1102-1111.
5. Orrell, M., Aguirre, E., Spector, A., Hoare, Z., Woods, R. T., Streater, A., ... & Russell, I. (2014). Maintenance cognitive stimulation therapy for dementia: single-blind, multicentre, pragmatic randomised controlled trial. *British Journal of Psychiatry*, *204*(6), 454-461.

Guidelines

National Institute for Health and Care Excellence (NICE) (2006) Supporting people with dementia and their carers in health and social care. (CG42) London: National Institute for Health and Care Excellence. http://www.nice.org.uk/guidance/cg42/resources/guidance-dementia-pdf

Scottish Intercollegiate Guidelines Network (SIGN). (2006) Management of patient with dementia. A national clinical guideline. CG86. Edinburgh: Scottish Intercollegiate Guidelines Network. http://www.sign.ac.uk/pdf/sign86.pdf

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Woods et al. (2012)	06/12/2011	*Participants*: Patients with dementia. The main diagnostic categories included were Alzheimer's disease and vascular dementia. Those including mild cognitive impairment were excluded. *Intervention*: Cognitive stimulation, an intervention for people with dementia which offers a range of enjoyable activities providing general stimulation for thinking, concentration and memory usually in a social setting, such as a small group. *Comparator*: No treatment, standard treatment, or placebo. *Outcome*: Primary outcomes: cognitive performance (Mini-Mental State Exam, MMSE; Alzheimer's Disease Assessment Scale – Cognitive, ADAS-Cog), quality of life, everyday functioning, behaviour, social engagement and neuropsychiatric symptoms. Carer outcomes; well-being, depression, anxiety, burden, strain, coping and satisfaction. *Study design*: RCT	15 (9 were new publications and 6 had been included in an earlier review by the authors)	This review aimed to assess the effectiveness of cognitive stimulation interventions for improving cognition in people with dementia. Seven studies were conducted in residential care settings, six studies included only community-dwelling participants, and two studies were conducted in mixed populations. The duration of the intervention ranged from 4 weeks to 24 months and session lengths range from 30 to 90 minutes. *Cognitive function*: The results of an overall meta-analysis indicated that cognitive stimulation interventions were associated with a statistically significant post-treatment improvement in cognition (SMD 0.41 (95% CI: 0.25 to 0.57)), based on 14 studies using a variety of outcome	The review reported a clear objective and defined appropriate inclusion criteria. A range of bibliographic databases were searched for relevant studies, however, the restriction to published studies, reported in English may have resulted in relevant data being omitted. The review process included measures

				measures. Data from two studies indicated no significant effect on cognitive function at 10 months follow-up. *Communication*: Cognitive stimulation interventions were found to have a statistically significant positive effect of staff ratings of communication and social interaction (SMD 0.44 (95% CI: 0.17 to 0.71)), based on data from four studies. Data from one study indicated no significant effect on communication and social interaction at 10 months follow-up. *Quality of life*: Data from four studies indicated that cognitive stimulation interventions were associated with improvements in quality of life, as measured by QoL-AD, (SMD 0.38 (95% CI: 0.11 to 0.65)). Data from the Chapman 2004 study (see Cooper 2012, above) were not included in this analysis, but were reported separately; this study found no significant effect of cognitive stimulation of QoL-AD at 10 months follow-up (SMD 0.34 (95% CI: -0.19 to	to minimise error/bias (i.e. involvement of two reviewers) throughout. The methodological quality of included studies was assessed using an appropriate tool. Meta-analytic pooling of studies, which used a wide variety of interventions, comparators, outcome measures and study durations is of questionable validity.

				0.88)). *Other outcomes*: No treatment effects were found for mood, activities of daily living, general behaviour function, or problem behaviour.	

Randomised controlled trials

Author (year)	**Inclusion criteria**	**Number of participants**	**Summary of results**	**Risk of bias**
Mapelli et al. (2013)	*Participants*: Patients with Alzheimer's disease (AD), recruited from a nursing home. Inclusion criteria: stage 1 or 2 on the Clinical Dementia Rating Scale (CDR); Mini-Mental State Examination (MMSE) score of 14-24; ability to take part. Exclusion criteria: suffering from a learning disability or psychiatric or internal disorder. *Intervention*: Cognitive Stimulation Therapy (CST); 40 one hour sessions, delivered daily over eight weeks. Therapy comprised initial personal, spatial, and temporal orientation sessions followed by individual exercises specific for five areas (memory, language, spatial and temporal	*n* = 30: 10 intervention (CST); 10 placebo (occupational therapy); 10 control (usual activities in the nursing home)	This study aimed to assess the effectiveness of a structured cognitive stimulation treatment to improve cognition and behavioural symptoms in people with dementia. Sixteen of the included participants had a diagnosis of AD, 13 had a diagnosis of vascular dementia and one had mixed dementia. Each of the three groups (intervention, placebo and control) included five participants with moderate dementia (MMSE 14-18) and five participants with mild dementia (MMSE 19-24). The mean age of study participants was approximately 84 years. There were no significant differences in demographic characteristics, or baseline clinical measures, between the three groups. No study participants were lost to follow-up and all were included in the analyses.	No details of randomisation method, or allocation concealment were reported. The nature of the interventions precluded blinding of study participants and personnel.

	orientation, attention, and logic) and grouped into three levels of difficulty. *Comparator*: (1) Placebo, treated with occupational therapy; 40 one hour sessions, delivered daily over eight weeks. Therapy comprised a series of programmed activities: read and debate the newspaper, play bingo, sing, and take part in PET therapy, psychomotor stimulation and creative workshops. The activities were changed every day and were adapted according to the degree of dementia. (2) Control, continuing with usual activities in the nursing home. *Outcome*: dementia severity (CDR); cognitive functions (MMSE; Esame Neuropsicologico Breve 2 (ENB2); activities of daily living (Activities of Daily Living Scale, ADLS); problem behaviours (Behavioural Pathology in Alzheimer's Disease Rating Scale, BEHAVE-AD); depression (Geriatric Depression Scale, GDS)		*Cognitive function*: After eight weeks of treatment, the CST group had significantly better performances than both the placebo and control groups for MMSE score ($F(2, 24) = 11.57$; $p < 0.001$) and for the following subsets of ENB2: immediate recall prose memory ($F(2, 24) = 4.92$; $p < 0.05$); delayed recall prose memory ($F(2, 24) = 7.58$; $p < 0.05$); clock drawing test ($F(2, 24) = 15.15$; $p < 0.001$) and abstraction ($F(2, 24) = 8.91$; $p < 0.05$) and ENB2 total score ($F(2, 24) = 14.06$; $p < 0.001$). The placebo and control groups showed no significant changes, from baseline to post-treatment, on any outcome measure. A similar pattern of results was observed for CDR score and behavioural outcome measures. No measures of long-term effectiveness (beyond the end of treatment) were reported.	Outcomes were assessed by a blinded rater, who did not know the group allocation of the participants. The rater was not the same person who conducted the intervention treatments. No study participants were lost to follow-up and all were included in the analyses. Results were reported for all listed outcome measures.
Maci et	**EXCLUDED – This study assessed a combined intervention, comprising cognitive stimulation, physical activity, and socialisation and does**			

al. (2012)	**not provide any information on the effectiveness of CST (any effects observed could be due to any or all of the components of the intervention).**			
Niu et al. (2010)	*Participants*: Patients with AD, recruited from a military sanatorium in Beijing, China. Inclusion criteria: diagnosis of probably AD according to NINCDS/ADRDA criteria; MMSE score between 10 and 24; Neuropsychiatric Inventory (NPI) score >5 points, arising from at least two domains of behaviour; no history of antidepressant medication. Exclusion criteria: severe hearing or visual impairments or disease that reduces functional abilities; history of psychotic disorders or substance abuse; medical conditions incompatible with study participation. *Intervention*: Individual cognitive stimulation therapy, focusing upon tasks requiring executive functions and working memory (reality orientation task, fluency task, overlapping figure task, photo-storey learning task), lasting 10 weeks. *Comparator*: Control group (individual mock intervention comprising tasks such as discussing topics and life events and learning about progress in current AD research and external memory aids that may be effective), lasting 10 weeks. *Outcome*: Neuropsychiatric symptoms	*n* = 32 (CST 16, control 16)	This study aimed to assess the effectiveness of CST for the treatment of neuropsychiatric symptoms in patients with Alzheimer's disease. There were no significant differences in demographic characteristics, or baseline clinical measures, between the intervention and control groups. The mean age of study participants was approximately 80 years and 78% were male. All study participants had been receiving a stable dose of a cholinesterase inhibitor (donepezil) for at least three months. One participant from each group withdrew consent during the study and one participant withdrew from the CST group due to admission to hospital; all participants were included in the analyses. *Cognitive function*: Participants in the CST group showed a greater improvement in MMSE score at week 10 (end of treatment) than those in the control group: mean change 0.81 points versus –0.19 points, t=3.106, P=0.004. Similar results were observed for total NPI score and for the apathy and depression/dysphoria domains of the NPI; there were no significant between group differences for any of the other domains of the NPI. No measures of long-term effectiveness (beyond the end of	Computerised block randomisation; no details of allocation concealment reported. The nature of the interventions precluded blinding of study participants and personnel. Outcomes were assessed blind to intervention group ("rater-blinded"). All study participants were included

	and cognition (Neuropsychiatric Inventory; MMSE)		treatment) were reported.	in the analyses. Results were reported for all listed outcome measures.
Orrell et al. (2014)	*Participants*: Patients with dementia, meeting DSM-IV criteria. Inclusion criteria: ability to communicate, hear and see well enough to participate. Exclusion criteria: major physical illness or disability/intellectual disability. *Intervention*: 24-week maintenance CST, after completion of a 7 week CST programme comprising 14, twice-weekly, 45 minute sessions. The maintenance programme was based upon the theory of cognitive stimulation as applied to the original programme. Maintenance CST was delivered in a group format; the format of the initial CST programme was not clear. *Comparator*: Treatment as usual (TAU), after completion of the same 7 week CST programme. *Outcome*: Cognitive abilities (Alzheimer's Disease Assessment Scale, ADAS-Cog; MMSE); quality of life (QoL-AD; Dementia Quality of Life Scale, DEMQOL); dementia	*n* = 236 (maintenance CST 123; TAU 113)	This study aimed to assess the effectiveness of maintenance CST in people with dementia. There were no significant differences in demographic characteristics, or baseline clinical measures, between the intervention and control groups. The mean age of study participants was approximately 83 years, 64% were female and 32% were receiving acetylcholinesterase inhibitors. Nine participants from each group were lost to follow-up at three months; 17 participants from the maintenance CTS group and 20 participants from the TAU group were lost to follow-up at six months. *Cognitive function*: There were no statistically significant differences in measures of cognitive function (MMSE or ADAS-Cog) between the CST maintenance and TAU groups, at 3 or 6 months follow-up. Modelling data indicated that, for people taking acetylcholinesterase inhibitors , the CST maintenance group showed less decline in MMSE at 3 and 6 months than the TAU group.	Remote randomisation, with allocation list stored under a secure password. The nature of the interventions precluded blinding of study participants and personnel. Outcomes were assessed blind to intervention group.

	behaviours (Neuropsychiatric Inventory); activities of daily living (Alzheimer's Disease Cooperative Study – Activities of Daily Living, ADCS-ADL). Outcomes were assessed at 3 and 6 months follow-up.		*Quality of life*: Participant reported quality of life measures were inconsistent at 3 months follow-up: QoL-AD indicated a better quality of life for participants in the CST maintenance group than for those in the TAU group (mean difference 1.78 (95% CI: 70.01 to 3.57), p=0.03), whilst DEMQOL indicated no significant difference. There were no significant between group differences, on either measure, at 6 months follow-up. Proxy quality of life measures (reported by family or care givers) indicated no significant between group differences at 6 months follow-up and significantly better quality of life for the CST maintenance group, on both measures, at 6 months: mean difference proxy QoL-AD 1.53 (95% CI: 0.37 to 2.69), p=0.01; mean difference proxy DEMQOL 3.24 (95% CI: 0.29 to 6.19), p=0.03. There were no significant between group differences in NPI or ADCS-ADL at 3 months follow-up, or in NPI at 6 months follow-up. ADCS-ADL scores favoured the CST maintenance group at 6 months follow-up.	Analyses were on an intension-to-treat basis Results were reported for all listed outcome measures.

Risk of bias

Systematic reviews

Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Woods et al. (2012)	☺	☹	☺	☺	☹

Randomised controlled trials

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Mapelli et al (2013)	?	?	☹	☺	☺	☺
Maci et al. (2012)	**EXCLUDED – This study assessed a combined intervention, comprising cognitive stimulation, physical activity, and socialisation and does not provide any information on the effectiveness of CST (any effects observed could be due to any or all of the components of the intervention).**					
Niu et al. (2010)	☺	?	☹	☺	☺	☺
Orrell et al. (2014)	☺	☺	☹	☺	☺	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

Search details

Source	Search Strategy	Number of hits	Relevant evidence identified
SRs and Guidelines			
NICE	Dementia	63	2
DARE	(dement* OR alzheimer*) IN DARE FROM 2012 TO 2014 230 Delete 2 MeSH DESCRIPTOR Alzheimer Disease EXPLODE ALL TREES 296 Delete 3 MeSH DESCRIPTOR Dementia EXPLODE ALL TREES 591 Delete 4 MeSH DESCRIPTOR Dementia, Multi-Infarct EXPLODE ALL TREES 0 Delete 5 MeSH DESCRIPTOR Dementia, Vascular EXPLODE ALL TREES 21 Delete 6 MeSH DESCRIPTOR Frontotemporal Dementia EXPLODE ALL TREES 3 Delete 7 MeSH DESCRIPTOR Lewy Body Disease EXPLODE ALL TREES 6 Delete 8 (reality ADJ2 orientation) IN DARE FROM 2012 TO 2014 2 Delete 9 ((memory OR cognitive OR global OR reality) ADJ2 (therap* OR group* OR support* OR stimulat* OR psycho-stimulat* OR psychostimulat* OR orientation)) IN DARE FROM 2012 TO 2014 276 Delete 10 MeSH DESCRIPTOR Reality Therapy EXPLODE ALL TREES 2 Delete 11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 678 Delete 12 #8 OR #9 OR #10 277 Delete 13 #11 AND #12	43	
Primary studies			
CENTRAL	#1 dementia or alzheimer:ti,ab,kw 8155 #2 MeSH descriptor: [Dementia] explode all trees 3814 #3 #1 or #2#1 or #2 8335 #4 reality near orientation 45 #5 cognitive near stimulation 277 #6 global near stimulation23 #7 "stimulation exercise*"54 #8 "memory group"16	240	

	#9 memory near stimulation208 #10 memory near support265 #11 memory near therapy929 #12 {or #4-#11}1709 #13 #3 and #12 278 (240 in Central)		
PsycINFO	1. PsycINFO; exp DEMENTIA/; 49229 results. 2. PsycINFO; dementia.ti,ab; 40380 results. 3. PsycINFO; 1 OR 2; 59266 results. 4. PsycINFO; "cognitiv* stimul*".ti,ab; 481 results. 5. PsycINFO; "reality orientation".ti,ab; 261 results. 6. PsycINFO; (memory adj2 therapy).ti,ab; 160 results. 7. PsycINFO; "memory group*".ti,ab; 110 results. 8. PsycINFO; "memory support".ti,ab; 70 results. 9. PsycINFO; (memory adj2 stimulat*).ti,ab; 137 results. 10. PsycINFO; "global stimulation".ti,ab; 6 results. 11. PsycINFO; ("cognitive psycho-stimulation" OR "cognitive psychostimulation").ti,ab; 0 results. 12. PsycINFO; "stimulation exercise*".ti,ab; 18 results. 13. PsycINFO; 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12; 1220 results. 14. PsycINFO; 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12; 1220 results. 15. PsycINFO; 3 AND 14; 248 results. 16. PsycINFO; CLINICAL TRIALS/; 6943 results. 17. PsycINFO; random*.ti,ab; 121175 results. 18. PsycINFO; groups*.ti,ab; 348411 results. 19. PsycINFO; (doubl* adj3 blind*).ti,ab; 17473 results. 20. PsycINFO; (singl* adj3 blind*).ti,ab; 1526 results. 21. PsycINFO; EXPERIMENTAL DESIGN/; 8717 results. 22. PsycINFO; controlled.ti,ab; 75517 results. 23. PsycINFO; (clinical adj3 study).ti,ab; 7408 results. 24. PsycINFO; trial.ti,ab; 63951 results.	103	

	25. PsycINFO; "treatment outcome clinical trial".md; 25074 results. 26. PsycINFO; 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25; 537971 results. 27. PsycINFO; 15 AND 26; 103 results.		
Embase	28. EMBASE; exp DEMENTIA/; 228603 results. 29. EMBASE; dementia.ti,ab; 89822 results. 30. EMBASE; 28 OR 29; 240116 results. 31. EMBASE; "cognitiv* stimul*".ti,ab; 637 results. 32. EMBASE; "reality orientation".ti,ab; 234 results. 33. EMBASE; (memory adj2 therapy).ti,ab; 160 results. 34. EMBASE; "memory group*".ti,ab; 127 results. 35. EMBASE; "memory support".ti,ab; 47 results. 36. EMBASE; (memory adj2 stimulat*).ti,ab; 426 results. 37. EMBASE; "global stimulation".ti,ab; 35 results. 38. EMBASE; ("cognitive psycho-stimulation" OR "cognitive psychostimulation").ti,ab; 1 results. 39. EMBASE; "stimulation exercise*".ti,ab; 65 results. 40. EMBASE; 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39; 1688 results. 41. EMBASE; 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39; 1688 results. 42. EMBASE; 30 AND 41; 505 results. 43. EMBASE; random*.tw; 900118 results. 44. EMBASE; factorial*.tw; 23315 results. 45. EMBASE; placebo*.tw; 202025 results. 46. EMBASE; (crossover* OR cross-over*).tw; 69842 results. 47. EMBASE; (doubl* adj3 blind*).tw; 143636 results. 48. EMBASE; (singl* adj3 blind*).tw; 17076 results. 49. EMBASE; assign*.tw; 242053 results. 50. EMBASE; allocat*.tw; 85229 results. 51. EMBASE; volunteer*.tw; 177796 results. 52. EMBASE; CROSSOVER PROCEDURE/; 40222 results. 53. EMBASE; DOUBLE-BLIND PROCEDURE/; 115438 results.	143	

	54. EMBASE; SINGLE-BLIND PROCEDURE/; 18827 results. 55. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 350056 results. 56. EMBASE; 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55; 1432748 results. 57. EMBASE; 42 AND 56; 143 results.		
Cinahl	58. CINAHL; exp DEMENTIA/; 34723 results. 59. CINAHL; dementia.ti,ab; 20194 results. 60. CINAHL; 58 OR 59; 38064 results. 61. CINAHL; "cognitiv* stimul*".ti,ab; 145 results. 62. CINAHL; "reality orientation".ti,ab; 119 results. 63. CINAHL; (memory adj2 therapy).ti,ab; 41 results. 64. CINAHL; "memory group*".ti,ab; 17 results. 65. CINAHL; "memory support".ti,ab; 18 results. 66. CINAHL; (memory adj2 stimulat*).ti,ab; 24 results. 67. CINAHL; "global stimulation".ti,ab; 2 results. 68. CINAHL; ("cognitive psycho-stimulation" OR "cognitive psychostimulation").ti,ab; 1 results. 69. CINAHL; "stimulation exercise*".ti,ab; 15 results. 70. CINAHL; 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69; 371 results. 71. CINAHL; 60 AND 70; 158 results. 72. CINAHL; random*.ti,ab; 112563 results. 73. CINAHL; groups*.ti,ab; 139891 results. 74. CINAHL; (doubl* adj3 blind*).ti,ab; 13933 results. 75. CINAHL; (singl* adj3 blind*).ti,ab; 2403 results. 76. CINAHL; controlled.ti,ab; 65088 results. 77. CINAHL; (clinical adj3 study).ti,ab; 10559 results. 78. CINAHL; trial.ti,ab; 67623 results. 79. CINAHL; 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78; 263861 results. 80. CINAHL; 71 AND 79; 53 results.	53	
Medline	81. MEDLINE; exp DEMENTIA/; 123516 results. 82. MEDLINE; dementia.ti,ab; 69226 results. 83. MEDLINE; 81 OR 82; 145333 results.	144	

	84. MEDLINE; "cognitiv* stimul*".ti,ab; 481 results. 85. MEDLINE; "reality orientation".ti,ab; 204 results. 86. MEDLINE; (memory adj2 therapy).ti,ab; 132 results. 87. MEDLINE; "memory group*".ti,ab; 96 results. 88. MEDLINE; "memory support".ti,ab; 42 results. 89. MEDLINE; (memory adj2 stimulat*).ti,ab; 343 results. 90. MEDLINE; "global stimulation".ti,ab; 34 results. 91. MEDLINE; ("cognitive psycho-stimulation" OR "cognitive psychostimulation").ti,ab; 2 results. 92. MEDLINE; "stimulation exercise*".ti,ab; 52 results. 93. MEDLINE; 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90 OR 91 OR 92; 1350 results. 94. MEDLINE; 83 AND 93; 328 results. 95. MEDLINE; "randomized controlled trial".pt; 388780 results. 96. MEDLINE; "controlled clinical trial".pt; 89842 results. 97. MEDLINE; randomi?ed.ab; 370467 results. 98. MEDLINE; placebo.ab; 159750 results. 99. MEDLINE; "drug therapy".fs; 1744944 results. 100. MEDLINE; randomly.ab; 222876 results. 101. MEDLINE; trial.ab; 321609 results. 102. MEDLINE; groups.ab; 1405833 results. 103. MEDLINE; 95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102; 3456929 results. 104. MEDLINE; 94 AND 103; 144 results.		
Summary	**NA**	**NA**	

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