



Is Supervised Cognitive Retraining Superior To Home-based Cognitive Rehabilitation In Early Alzheimer's Disease (AD) Dementia?

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Key message: Open-labelled trial evidence → Structured aptitude-based CR was not superior to a pragmatic home-based rehabilitation strategy for improving longitudinal cognitive trends in early AD, with both groups demonstrating relative stability. In the era of monoclonal antibodies, the impact of biologicals on test scores and CDR-SB should be compared with an active HR/CR arm to reliably determine real-world efficacy, rather than limiting to a placebo-controlled arm.

INTRODUCTION

- Interventions during the early stages of AD can potentially mitigate the rate of decline and preserve activities of daily living.
- Objective: To establish efficacy of Supervised Aptitude-based Cognitive Retraining strategy in Early AD Dementia (SACRED trial) in comparison to active home-based rehabilitation

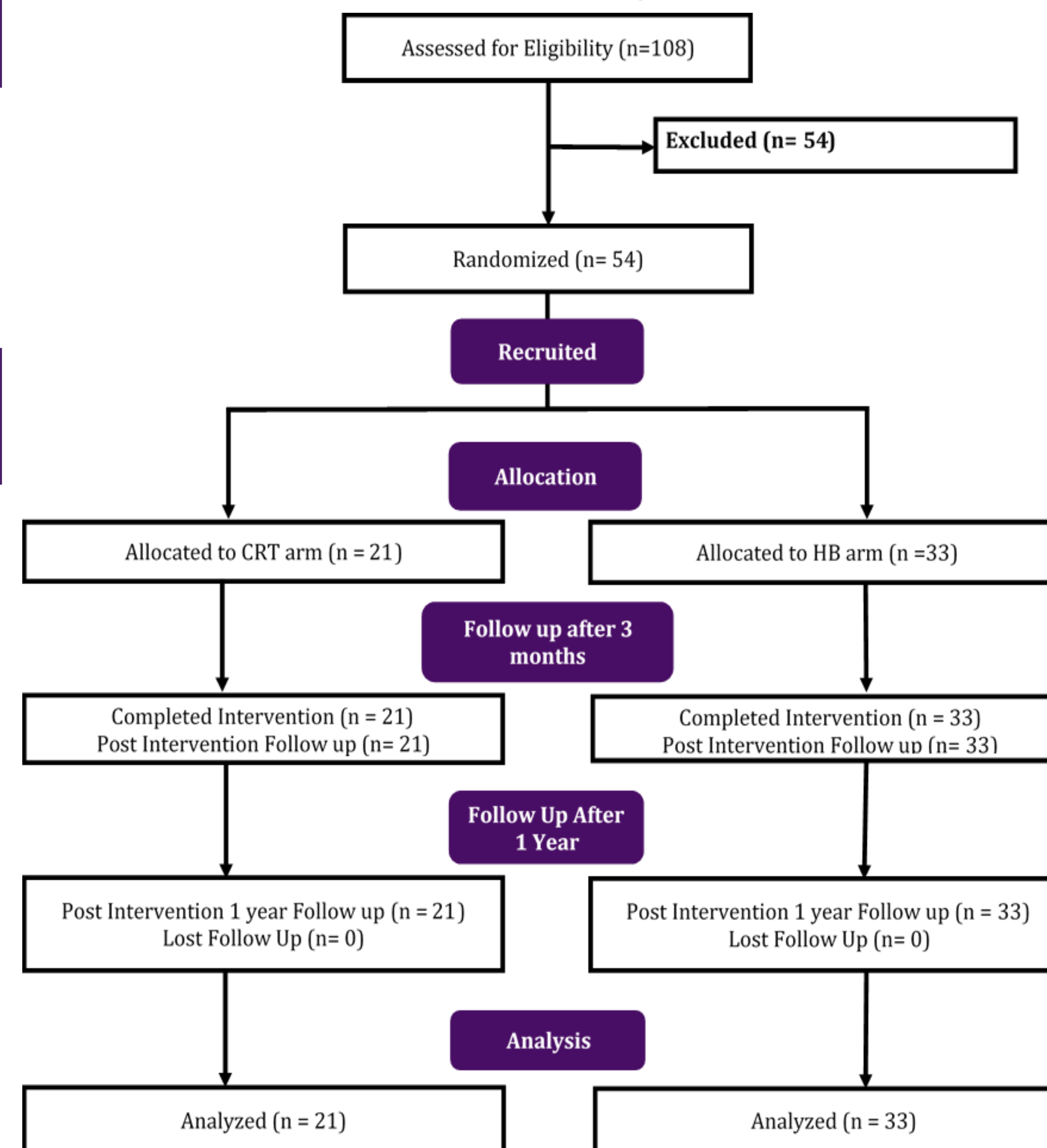
METHODOLOGY

- N=54 early AD; CDR<2 (after completion of neuropsychological and imaging evaluations at baseline, post-intervention at 3 months and at one year while on best medical management.
- Clinical Dementia Rating-sum of boxes (CDR-SB) scales and activities of daily living (ADL) were also assessed.
- The neurologist was blinded to the allocation arms.
- Baseline MRI volumetric measures analyzed using SPM version 12.

WEEK 1	Trail Making, Letter Cancellation, Letter-Number Substitution, Object Manipulation, Sentence Repetition, Dual Encoding
WEEK 2	Trail Making, Letter Cancellation, Letter-Number Substitution, Grain Sorting, Maze, Bead Categorisation, Following Directions, Sight Word reading, Dual Encoding, Random Object Picture Memory
WEEK 3	Trail Making, Letter Cancellation, Letter-Number Substitution, Grain Sorting, Maze, Bead Categorisation, Visual Closure, Following Directions, Phonetic Word Reading, Dual Encoding
WEEK 4	Letter Cancellation, Letter-Number Substitution, Grain Sorting, Word Generation, Maze, Card Sorting, Visual figure ground, Naming and Describing things
WEEK 5	Symbol Cancellation, Letter-Symbol Substitution, Grain Sorting, Rearranging Jumbled Letters, Word Generation Letter Switching, Start Stop Task, Maze, Card Sorting, Dot based figure construction, Visual Figure ground, Word List Retention, Memory of Location
WEEK 6	Symbol Cancellation, Letter-Symbol Substitution, Grain Sorting, Rearranging Jumbled words, Word generation-combination, Start Stop Task, Stroop, Planning Events, Visual Construction-matchsticks, Embedded Shape, Memory of Location
WEEK 7	Symbol Cancellation, Letter-Symbol Substitution, Rearranging Jumbled words, Planning Events, Motor Set Shift Task, Construction of Symmetric designs, Similarity, Memory of Design
WEEK 8	Symbol Cancellation, Letter Symbol substitution, Colour Object Matching -familiar, Planning-Essay, Motor set shift, Construct symmetric design, Proverb Illustration, Memory of Design
WEEK 9	Paired Letter Cancellation, Colour Object Matching -unfamiliar, Recall Complex pictures, Proverb Illustration
WEEK 10	Paired Symbol Cancellation, Picture Memory,[repeating tasks that the participant had difficulty with]
WEEK 11	Paragraph Retention, Circle A cancel O[repeating tasks that the participant had difficulty with]
WEEK 12	Paragraph Retention,[repeating tasks that the participant had difficulty with]

1. Daily Routine setting and Weekly Planning		CRT (n = 21)	HR (n = 33)	t	p
2. Diary Writing		Mean (S.D)	Mean (S.D)		
3. Reminiscence Therapy	Age	71.81 (4.38)	68.97 (6.53)	1.75	.08
4. Reality Orientation	Education in Years	13.52 (3.37)	12.87 (2.48)	0.75	.45
5. Organizing	Sex (M / F)	8 / 13	21 / 12	-	-
6. Environmental Modifications	Baseline ACE- III Total	77.90 (9.55)	75.42 (11.28)	.83	.41
7. Creating Location Charts with symbols and Pictures	Baseline CDR Total	3.38 (1.58)	4.19 (1.86)	-1.66	.10
8. Visual Reproduction Exercises	Baseline IADL CDI	18.60 (10.40)	25.88 (18.49)	-1.84	.07
9. Encouraging Hobbies and Interests	Baseline IADL PDI	1.43 (2.81)	3.54 (6.85)	-1.57	.12

CONSORT diagram

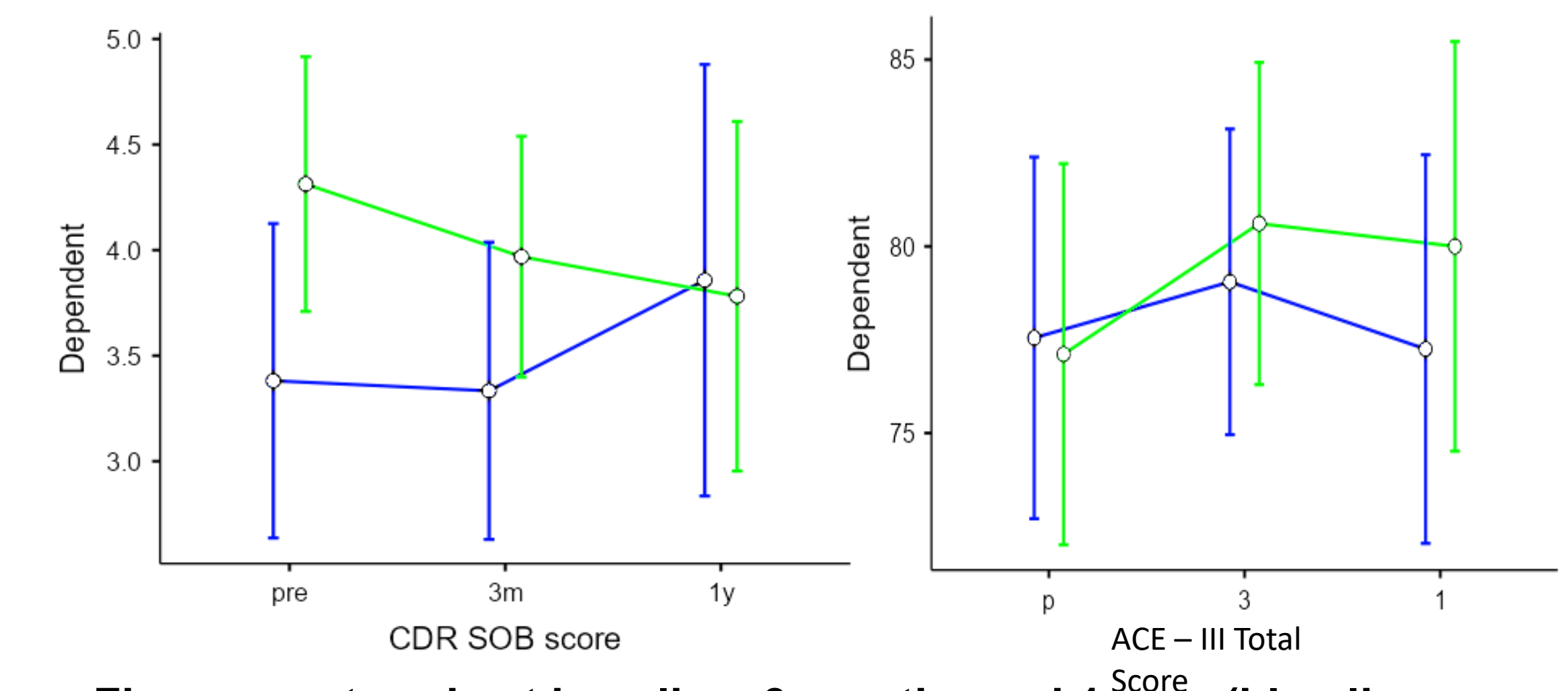


RESULT

- 21 participants opted for a psychologist-supervised validated cognitive retraining (CR) protocol (60-minute sessions once weekly for 12 weeks), and 33 for home-based caregiver-supervised cognitive rehabilitation (HR) program (60min sessions daily).
- No significant between group (CR vs HR) differences were observed in baseline age or education status, total ACE, IADL, SF-36, memory or depression subscores. (Table)
- Significant trajectories for improvements in CDR-SB (p=0.04), category fluency (p=0.048), paragraph learning (p=0.003) visuospatial scores (p=0.048) in the HR subgroup over 1 year.
- Significant within group improvements on phonemic fluency (p=0.007), list recognition memory (p=0.024), reduced list omission errors (p=0.025), trail making test-A time (p<0.001), anxiety and depression sub-scores (p=0.012) on HADS.
- Higher baseline grey matter, right parahippocampal and white matter volumes were associated with lower likelihood of decline on ACE language and memory sub-scores respectively

Table: Trends of trajectory of cognitive changes and CDR between groups-repeated measure ANOVA

Variable	Time point	Mean for CR	Mean for HR	p
CDR SOB Score	Baseline	3.38	4.31	0.04
	3 months	3.33	3.97	
	1 year	3.86	3.78	
ACE III Category fluency	Baseline	4.65	4.11	0.048
	3 months	4.40	4.33	
	1 year	4.05	4.39	
ACE III Visuospatial	Baseline	13.2	11.8	0.048
	3 months	13.5	12.4	
	1 year	12.6	12.4	
WMS LM Immediate recall	Baseline	9.00	7.62	0.003
	3 months	9.35	11.25	
	1 year	7.25	11.81	
WMS PAL Hard Total(B)	Baseline	1.75	1.56	0.051
	3 months	1.40	2.44	
	1 year	1.40	2.44	



CONCLUSION

- Both CR and HR are efficacious in slowing the rate of cognitive decline in early AD with relative improvements in HR sub-scores on CDR-SB and limited domain-specific measures above CR
- Within group improvements noted on domain-specific measures apparent in both arms on fluency, memory, psychomotor speed, anxiety and depression measures.
- Cognitive trajectory post intervention appears to be independent of baseline MRI volumes

REFERENCES

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- Bahar-Fuchs A, Clare L, Woods B. Cognitive training and cognitive rehabilitation for mild to moderate Alzheimer's disease and vascular dementia. Cochrane Database Syst Rev. 2013 Jun 5;2013(6):

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