

Best Evidence Summaries of Topics in Mental Healthcare

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

Question

“In adults with schizophrenia, how effective is cognitive remediation therapy, compared to treatment as usual, in improving patient outcomes?”

Clarification of question using PICO structure

<i>Patients:</i>	Adults with schizophrenia
<i>Intervention:</i>	Cognitive remediation therapy
<i>Comparator:</i>	Treatment as usual
<i>Outcome:</i>	Improving patient outcomes

Clinical and research implications

One systematic review and three additional RCTs reported results indicating that cognitive remediation may have a positive effect on cognitive function when used to treat patients with schizophrenia. However, all four studies had significant methodological flaws and the evidence remains weak. The same four studies also provided weak evidence that cognitive remediation may have positive effects on life skills, social functioning and symptoms. One further, high quality RCT found no significant differences in effectiveness between cognitive remediation and Cognitive Behavioural Therapy for improving psychological and depressive symptoms in people with schizophrenia. Further, larger, high quality studies are needed to confirm or refute the findings reported by the studies included in this evidence summary.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified one systematic review,¹ and four additional randomised controlled trials (RCTs),^{2,3,4,5} which reported data relevant to this evidence summary. The systematic review included 40 comparative studies of cognitive remediation in people with schizophrenia, but did not specify a comparator or reported details of the cognitive remediation interventions and comparators used in individual studies.¹ Three additional RCTs compared cognitive remediation with non-psychological interventions: leisure-based group activities,² group psychoeducation,³ and physical exercise.⁵ One further RCT compared cognitive remediation with cognitive behavioural therapy (CBT).⁴ All studies were conducted in participants with schizophrenia and all included an assessment of cognitive function and a variety of additional outcome measures (e.g. life skills, functional outcomes, symptoms) were reported by various studies.

Main Findings

The systematic review found that cognitive remediation improved measures of cognitive skills, reporting a pooled effect estimate, post-treatment, of 0.45 (95% CI: 0.31 to 0.59); a medium effect size.¹ The also article stated that “there was a significant small-to-medium effect on functioning outcomes at both post-treatment and follow-up assessment.¹ There was also a small, significant effect of cognitive remediation on symptoms at post-treatment.¹” However, no numerical data were presented to support these statements. All three RCTs that compared cognitive remediation to non-psychological therapies found statistically significant treatment effects on measures of cognitive function, in favour of cognitive remediation.^{2,3,5} One of these RCTs reported a numerical estimate of treatment effect for the Behavioural Assessment of dysexecutive Syndrome (BADS) score (0.43 (95% CI: 0.10 to 0.70)).² Two of the three RCTs also reported statistically significant treatments effects on measures of life skills and social functioning, in favour of cognitive remediation;^{2,5} the third study did not assess these outcomes.³ Two of the three studies found that cognitive remediation was associated with significantly greater improvements in symptoms (Positive and Negative Syndrome Scale (PANSS) than comparator treatments.^{3,5} The final RCT, which compared cognitive remediation to CBT found no significant differences on any outcome measure (modified PANSS, Calgary Depression Rating Scale for Schizophrenia (CDSS), Clinical Global Impression Scale (CGI), or the Symptom Checklist (SCL-90-R)).⁴

Authors Conclusions

One systematic review concluded that cognitive remediation benefits people with schizophrenia, and when combined with psychiatric rehabilitation. Three additional RCTs concluded that cognitive remediation is beneficial when compared to group activity sessions, psychoeducation, or physical exercise training. One further RCT found no significant differences in treatment effects between CBT and cognitive remediation.

Reliability of conclusions/Strength of evidence

One systematic review, with significant methodological weaknesses, reported an overall treatment effect which indicated a positive effect on cognitive function when cognitive remediation was used to treat patients with schizophrenia.¹ However, neither the details of the cognitive remediation therapies, or the comparator treatments/controls, used in the individual studies were reported; the overall effect estimate is therefore of questionable validity and is unlikely to be reliable.¹ Three additional, small RCTs all reported statistically significant treatment effects on measures of cognitive function, when cognitive remediation was compared to various non-psychological interventions.^{2,3,5} These RCTs add some weight to the hypothesis that cognitive remediation may have positive effects on cognitive function in people with schizophrenia, but the evidence remains weak. The same three RCTs provided some data indicating that cognitive remediation may also have positive effects on life skills, social functioning and symptoms.^{2,3,5} One further, high quality RCT found no significant differences in effectiveness between cognitive remediation and CBT.⁴

What do guidelines say?

NICE Guidelines for schizophrenia (2010, CG82) provide the following definition of cognitive remediation;

“Cognitive remediation was defined as:

- an identified procedure that is specifically focused on basic cognitive processes, such as attention, working memory or executive functioning, and
- having the specific intention of bringing about an improvement in the level of performance on that specified cognitive function or other functions, including daily living, social or vocational skills.” (pp. 276).

It continues;

“The previous guideline found no consistent evidence for the effectiveness of cognitive remediation versus standard care or any other active treatment in improving targeted cognitive outcomes or other critical outcomes, such as symptom reduction.

Although limited evidence of efficacy has been found in a few recent well conducted studies, there is a distinct lack of follow-up data and various methodological problems in the consistency with which outcomes are reported. Where studies comprehensively reported outcomes at both ends of treatment and follow-up, there was little consistent advantage of cognitive remediation over standard care and attentional controls. Consequently, although there are some positive findings, the variability in effectiveness suggests that the clinical evidence as a whole is not robust enough to change the previous guideline.

The GDG did note, however, that a number of US-based studies have shown sustained improvements in vocational and psychosocial outcomes when cognitive remediation is added to vocational training and/or supported employment services.” (pp. 282)

The studies included in this evidence summary are not adequate to change the conclusions reached in current guidelines.

Date question received: 14/11/2013

Date searches conducted: 18/11/2013

Date answer completed: 09/12/2013

References

Systematic Reviews

1. Wykes et al (2011). A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes. (Am J Psychiatry 2011; 168:472–485)

Randomised Controlled Trials

2. Gharaeipour, M. and B. J. Scott (2012). "Effects of cognitive remediation on neurocognitive functions and psychiatric symptoms in schizophrenia inpatients." Schizophrenia Research 142(1-3): 165-170.
3. Farreny, A., et al. (2012). "REPYFLEC cognitive remediation group training in schizophrenia: Looking for an integrative approach." Schizophrenia Research 142(1-3): 137-144.
4. Klingberg, S., et al. (2011). "The role of cognitive behavioral therapy and cognitive remediation for the treatment of negative symptoms." European archives of psychiatry and clinical neuroscience 261.
5. Tan, B. L. and R. King (2013). "The effects of cognitive remediation on functional outcomes among people with schizophrenia: A randomised controlled study." Australian & New Zealand Journal of Psychiatry 47(11): 1068-1080

Clinical Guidelines

6. National Institute for Health and Care Excellence (2010) Schizophrenia. Core intervention in the treatment and management of schizophrenia in adults in primary and secondary care (updated edition). CG82. London: National Institute for Health and Care Excellence.
<http://www.nice.org.uk/nicemedia/live/11786/43607/43607.pdf>

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Wykes et al. (2011)	June 2009	<p><i>Participants:</i> Included studies were required to have ≥70% of participants with a diagnosis of schizophrenia, and all participants had to be receiving standard care, including appropriate medication.</p> <p><i>Intervention:</i> An intervention fulfilling the standard Cognitive Remediation Experts Workshop definition for cognitive remediation.</p> <p><i>Comparator:</i> Not specified</p> <p><i>Outcomes:</i> Cognitive or functional outcome distinct from the trained task.</p> <p><i>Study design:</i> Studies with a comparison group and allocation procedure</p>	39 reports of 40 studies (total n=2,104 participants, range 10 to 145)	<p>This review aimed to assess the effectiveness of cognitive remediation therapy for schizophrenia.</p> <p>The overall mean age of study participants was 35.6 years (range 15.3 to 48.3), and the mean proportion of males was 67% (range 30% to 100%). 47% Of participants were inpatients and symptom severity was generally in the mild to moderate range, 5 though some studies included participants with more severe symptoms.</p> <p>31 Studies assessed individual remediation and 9 assessed group therapy. Twenty-one studies used drill and practice, and 19 used drill plus strategy. 25% of studies involved the use of drill and practice exercises on a computer, without additional psychiatric rehabilitation. The mean length of treatment was 32.2 hours (range 4 to 130) over a mean of 16.7 weeks (range 2 to 104). The mean therapy intensity was 2.2 sessions per week (range 0.6 to 5).The article stated that 14</p>	<p>This review reported a clear research objective and defined broad inclusion criteria.</p> <p>Bibliographic databases and reference screening were used to identify potentially relevant studies and non-English speaking experts were contacted too identify additional studies. However, only studies with an English language abstract were included, raising the possibility of language bias and potential omission</p>

				<p>different treatments were represented and these were not described in detail. No details of the comparator treatment(s) were reported.</p> <p>The pooled estimate of effect size, for cognitive skills post-treatment, was 0.45 (95% CI: 0.31 to 0.59); a medium effect size.</p> <p>The article stated that “there was a significant small-to-medium effect on functioning outcomes at both post-treatment and follow-up assessment. There was also a small, significant effect of cognitive remediation on symptoms at post-treatment.” However, no numerical data were presented to support these statements.</p> <p>Regression analysis found no significant moderator variables. The authors reported the results of further exploratory analyses (not specified in the methods section): In studies that provided cognitive remediation therapy as an adjunct to psychiatric rehabilitation, the effect size was 0.59 (95% CI: 0.30 to 0.88), compared to 0.28 (95% CI: -0.02 to 0.58), for cognitive remediation alone. Similarly, a significant treatment effect was apparent only when a ‘drill plus</p>	<p>of relevant studies.</p> <p>Data extraction and assessment of the methodological quality of the included studies involved two reviewers, however, it was not clear whether study selection involved similar measures to minimise error and/or bias.</p> <p>Overall effect sizes (Cohen’s d) were calculated for cognitive skill and functional differences. These effect measures were calculated despite clear clinical and statistical heterogeneity between studies.</p>
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				strategy' approach was used and not for studies using 'drill plus practice.'	Although some attempt was made to investigate sources of heterogeneity, the value of the pooled effect measures remains questionable.
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RCTs

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Farreny (2012)	<p><i>Population:</i></p> <p>Participants were eligible to take part in this study if: they had a diagnosis of schizophrenia or schizoaffective disorder and more than 2 years illness duration; they had completed primary studies or were able to successfully complete a reading comprehension task; they had an MMSE score ≥ 24 and Global Assessment of Functioning score between 40 and 70. Exclusion criteria were: acute illness exacerbation; intellectual disability or neurological disorder; participating in any psychological intervention different from usual care; need for switching of antipsychotic medication during or within</p>	n = 62 (34 REPYFLEC, 28 Control).	<p>This study aimed to evaluate the effectiveness of the authors' cognitive remediation group training intervention (REPYFLEC), for improving cognition and functioning in schizophrenia patients.</p> <p>The mean age of study participants was 40.6 ± 7.6 years and the mean illness duration was 17.5 ± 8.9 years. 68% Of study participants were male, 84% were single and 80% had completed at least 8 years of formal education. 89% Of participants had a diagnosis of schizophrenia, (paranoid-type n=35 and schizoaffective disorder n=7. During the year prior to the study, 80% of the participants had not engaged in any type of work, occupational or academic activity, and did not have responsibility for any household chores. There were statistically differences between the groups at baseline in socio-demographic, clinical, symptom or cognitive variables.</p>	<p>The article states that "participants were assigned through a randomised procedure," but no details of the randomisation process or allocation concealment are reported.</p> <p>The study was</p>

	<p>one month of the start of the trial; diagnosis of alcohol or drug dependence within one month of the start of the trial.</p> <p><i>Intervention:</i> REPYFLEC (cognitive remediation group training; problem solving and cognitive flexibility training), 32 sessions</p> <p><i>Comparison:</i> Group sessions of activities without specific learning objectives and focused upon leisure, 32 sessions</p> <p><i>Outcomes:</i> Outcomes concerned Cognition, (<i>Behavioural Assessment of dysexecutive Syndrome</i> (BADS). <i>The Trail Making Test</i> (TMT), <i>Wechsler Memory Scale-III</i> (WMS-III)).</p>		<p>Six participants from the intervention group and nine from the control group left the study before completion.</p> <p>REPYFLEC CR is a strategy-based training that targets executive function and metacognition. It was delivered in a group format (4–6 participants), over 4 months in twice weekly sessions (32 sessions of 1 h). Contents were divided into two main areas: Problem Solving (PS) and Cognitive Flexibility (CF).</p> <p>Outcomes were assessed at baseline, after 8 weeks of treatment, at 16 weeks (post-treatment), and at 40 weeks (follow-up).</p> <p>After 8 weeks of treatment, there were significant differences between the groups on any measure. At 16 weeks (post-treatment), a significant treatment effect was found on cognitive function total score (BADS) 0.43 (95% CI: 0.10 to 0.70); this effect was maintained at follow-up. Significant treatment effects were also seen at six weeks for measures of functioning (Life Skills Profile (LSP) 0.33 (95% CI: 0.06 to 0.60) and Social Functioning Scale (SFS) 0.32 (95% CI: 0.04 to 0.60)); these effects were also maintained at follow-up. There were no significant effects on overall psychiatric symptoms (Positive and Negative Syndrome Scale (PANSS)), either post-treatment, or at follow-up.</p>	<p>single blind; outcome assessors were unaware of group allocation until after the outcome assessment was complete.</p> <p>It was not clear whether all participants were included in the analyses, or how dropouts were accounted for.</p> <p>Results were reported for all specified outcomes, but no numerical values were given for non-significant results.</p>
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Gharaeipour (2012)	<p><i>Population:</i> Inpatients over the age of 20, with a diagnosis of schizophrenia as defined by the DSM-IV. Participants were excluded if presenting with auditory or visual impairment, mental retardation, history of traumatic brain injury, neurological illness, substance abuse or dependence.</p> <p><i>Intervention:</i> Cognitive Remediation exercises in 1 hour sessions 5 times per week for a period of 2 months.</p> <p><i>Comparison:</i> Group Supportive Therapy, utilising an illness management psychoeducational approach.</p> <p><i>Outcomes:</i> Neuropsychological tests: Rey Auditory Verbal Learning Test (RAVLT; Lezak, 2012) The Wisconsin Card Sorting Test (WCST; Heaton, 1981) Auditory Consonant Trigrams (ACT; Stuss et al., 1987) The Rey–Osterrieth Complex Figure Test (ROCF; Osterrieth, 1944; Rey, 1941) The Trail Making Test (TMT, Parts A and B; Army Individual Test Battery, 1944; Baer and Blais, 2010) assesses attention and processing speed. Psychiatric measures: The Positive and Negative Syndrome Scale (PANSS; Kay et</p>	n = 42 (n = 21 in the experimental group, n = 21 in the control group)	<p>This study aimed to assess the effects of cognitive remediation on neurocognitive performance, psychiatric symptoms, and depression and anxiety in people with schizophrenia.</p> <p>No significant baseline differences were found between the treatment and control groups on social and demographic variables, duration and severity of illness, or symptoms (PANSS, BDI, or BAI).</p> <p>The cognitive remediation program was made up of educational, experiential (trying out strategies) and reflective (group discussion) components. Treatment approximately 40 hours of neurocognitive exercises that provided equal practice time in areas of attention and concentration, learning and memory, and executive functions. The control group received group supportive therapy for the same time. The group supportive therapy used an illness management and education approach providing patients with psychoeducation about schizophrenia and teaching applied coping strategies.</p> <p>Cognitive function (neuropsychological tests): Significant treatment effects were found for cognitive remediation on TMT (A, B), ACT, RAVLT (trials 1–5), ROCF (copy, delayed), and WCST (categories completed, perseverative errors), but not for RAVLT (delayed recall).</p> <p>Symptoms: Significant treatment effects were found for cognitive</p>	<p>Randomisation was independently conducted by a research assistant not involved in the study treatments.</p> <p>No details of allocation concealment were reported.</p> <p>The study was single blind; outcome assessors were unaware of group allocation.</p> <p>All participants in both groups completed the program and no one dropped out of the study.</p>
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	al., 1988)The Beck Depression Inventory-II (BDI-II; Beck et al., 1996) The Beck Anxiety Inventory (BAI; Beck et al., 1988)		<p>remediation on the PANSS Negative subscale, but not on the Positive subscale. There was also a significant improvement in depressive symptoms, but not anxiety scores, associated with cognitive remediation therapy.</p> <p>No numerical difference values were reported (p values and mean baseline and endpoint values, by group, only).</p>	Data were reported for all specified outcomes.
Klingberg (2011)	<p><i>Population:</i> Inclusion criteria: A diagnosis of schizophrenia according to the DSM IV; at least one moderate negative symptom according to the modified scale PANSS-MNS ≥ 10; German speaking; outpatient; able & willing to provide informed consent.</p> <p>Exclusion criteria: Any PANSS positive symptom ≥ 6; any extrapyramidal symptom of at least moderate intensity; age < 18 or > 55; organic brain disease; diagnosis of substance abuse or dependence; travel time to the study centre of ≥ 1 hour.</p> <p><i>Intervention:</i> CBT (20 sessions over 9 months)</p> <p><i>Comparison:</i> Cognitive Remediation (20 sessions over 9 months)</p> <p><i>Outcomes:</i> The primary outcome for this study was a modified negative symptom score PANSS-MNS. Additional measures were: the Scale</p>	n = 198 (n = 99 CBT group, n = 99 CR group)	<p>This trial aimed to assess the effectiveness of CBT, compared to cognitive remediation (CR) for the control of negative symptoms in people with schizophrenia.</p> <p>There were no significant differences between the groups at baseline, on demographic and social variables, diagnosis, symptoms, or medication use.</p> <p>CBT applied general principles (e.g. case formulation based on a cognitive model, goal setting, discussion of cognitive processes, homework assignments, role-play) for the treatment of negative symptoms. CR was adapted from an earlier study and applied the principles of restitution as well as compensation; the program followed the principles of errorless learning, overlearning, and immediate positive feedback (verbal), combined with alternative cognitive strategies such as systematic elaboration of information, verbalisation, self-instruction, and structuring of information. All therapies were delivered by trained clinical psychologist.</p> <p>No statistically significant differences between the groups were observed for the primary outcome, or for any of the secondary measures. One of the three centres observed a</p>	A permuted block design with random blocks stratified by study centre was applied. The allocation sequence was generated by a central computer and the research assistant responsible for assessments reported inclusion of new patients by fax or email, with the result of






	<p>for the Assessment of Negative Symptoms S101 Results of the Randomized Clinical TONES Study (SANS); the standard negative scale of the PANSS; standard positive scale of the PANSS; the Calgary Depression Rating Scale for Schizophrenia (CDSS); the Clinical Global Impression Scale (CGI); the Symptom Checklist (SCL-90-R).</p>		<p>borderline significant effect, for the primary outcome, in favour of CR.</p> <p>No numerical difference values were reported (p values and mean baseline and endpoint values, by group, only).</p>	<p>randomisation returned only to the therapist in order to keep the assessor blind.</p> <p>The nature of the intervention precludes blinding of participants and study personnel, but the similar nature of the interventions means that participant blinding is unlikely to be an important factor.</p> <p>The study was single blind; outcome assessors were</p>
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				<p>unaware of group allocation.</p> <p>An intention-to-treat analysis was included and data were reported for all specified outcome measures.</p>
Tan (2013)	<p><i>Population:</i> Participants were eligible for inclusion in this study if they had a diagnosis of schizophrenia or schizo-affective disorder according to the DSM-IV. Participants with known neurological, cardiovascular, respiratory, and developmental diseases were excluded from the study. All participants had a Global Assessment Functioning score >30.</p> <p><i>Intervention:</i> Cognitive remediation, consisting of computer based exercises as well as cognitive-based counselling for up to 5 hours per week for 12 weeks. Participants also received one session of cognitive</p>	n = 70 (n= 36 experimental group, n = 34 control)	<p>This study aimed to assess the effectiveness of cognitive remediation, compared to a physical exercise programme, for improving neurocognition and functional outcomes in people with schizophrenia.</p> <p>There were no significant differences between the groups at baseline on demographic and social variables, diagnosis, disease severity, duration of illness, medication use, or measures of neurocognition. However, there were significant differences, favouring the exercise group in the Independent Living Scales (ILS) problem solving subscale and in the Multnomah Community Ability Scale (MCAS).</p> <p>Outcomes were assessed at baseline, after 3 months treatment, and after 6 months and 1 year follow-up.</p>	<p>Randomisation was done independently, using a computer generated sequence.</p> <p>The sequence was placed in numbered sealed Envelopes and participants were asked to pick an</p>

























	<p>based counselling fortnightly, and therapists continued to provide monthly support to participants in the use of cognitive strategies for a further 12 months.</p> <p><i>Comparison:</i></p> <p>Physical exercise (adapted from the Structured Exercise Programme implemented by the Centre for Psychiatric Rehabilitation at Boston University (Hutchinson et al., 2005). 5 hours per week for 12 weeks. The programme consisted of exercises in the gymnasium, as well as physical-based counselling.</p> <p><i>Outcomes:</i></p> <p>A battery of tests were used to assess neurocognitive and physical fitness, skills attained through the programme were also assessed. Functional outcomes were measured along with psychiatric measures and quality of life.</p>		<p>Ten participants in each group discontinued the intervention before completion of the programme. One participant from the cognitive remediation group and three from the physical exercise group were lost to follow-up.</p> <p><i>Neurocognition:</i></p> <p>The cognitive remediation group showed greater improvements over time than the physical exercise group on all measures (Comprehensive Trail Making Test (CTMT), Rey Auditory Verbal Learning Test (RAVLT), and Wechsler Adult Intelligence Scale (WAIS)-Digit Span Forward and Backward).</p> <p><i>Physical fitness:</i></p> <p>There was significantly greater improvement in Rockport Walking Test VO² max scores for the physical exercise group than for the cognitive remediation group.</p> <p><i>Skills attainment:</i></p> <p>The cognitive remediation group showed greater improvements over time than the physical exercise group on ILS and Work Behaviour Inventory (WBI).</p> <p><i>Functional outcomes:</i></p> <p>The cognitive remediation group showed significantly greater improvement community ability (MCAS) than the physical exercise group over the course of the study.</p> <p><i>Symptoms and quality of life:</i></p> <p>The cognitive remediation group had significantly better symptom recovery (PANSS total and PANSS negative</p>	<p>envelope.</p> <p>All therapists and participants were informed that the topic of the research study was 'The effects of CR and PE on functional outcomes among people with schizophrenia'.</p> <p>They were not told that the CR was the treatment that was being researched and that PE was the placebo treatment.</p> <p>Outcome</p>
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			<p>subscale) than the physical exercise group over the year of the study. However, there were no significant time by group effects on quality of life.</p>	<p>assessment was undertaken by therapists not involved in treatment.</p> <p>An intention-to-treat analysis was included.</p> <p>Full results were only reported for neurocognitive measures.</p>
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Risk of Bias: SRs


Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Wykes et al. (2011)					

RCTs

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Farreny (2012)						
Gharaeipour (2012)						
Klingberg (2011)						
Tan (2013)						

 Low Risk

 High Risk

 Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
<i>SRs and Guidelines</i>			
NICE	Psychosis AND cognitive (remediation Or enhancement OR rehabilitation)		
DARE	(cogniti* adj4 (remediat* OR enhance* OR rehab*)) IN DARE 68 Delete 2 (schizo*) IN DARE 591 Delete 3 (psycho*) IN DARE 3818 Delete 4 MeSH DESCRIPTOR Schizophrenia EXPLODE ALL TREES 457 Delete 5 MeSH DESCRIPTOR Psychotic Disorders EXPLODE ALL TREES 138 Delete 6 (bipolar OR mania OR manic OR hypomani*) IN DARE 247 Delete 7 (affective ADJ2 disorder*) IN DARE 135 Delete 8 (rapid ADJ2 cycling) IN DARE 12 Delete 9 MeSH DESCRIPTOR Bipolar Disorder EXPLODE ALL TREES 149 Delete 10 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 4439 Delete 11 #1 AND #10	39	
<i>Primary studies</i>			
CENTRAL	#1 "cognitive remediation":ti,ab,kw 105 #2 "cognitive enhancement""cognitive enhancement" 99 #3 "cognitive rehabilitation""cognitive rehabilitation" 194 #4 "cognitive training""cognitive training" 270 #5 "neurocognitive remediation""neurocognitive remediation" 7 #6 #1 or #2 or #3 or #4 or #5 611 #7 schizophrenia or psychosis or psychotic 11305 #8 MeSH descriptor: [Schizophrenia] 4585 #9 MeSH descriptor: [Psychotic Disorders] 1414 #10Enter terms for search#7 or #8 or #9 11305 #11Enter terms for search#6 and #10 209	56	

	#12 date limit 2010-2013 = 56		
PsycINFO	1. PsycINFO; (cognitive adj3 remediation).ti,ab; 606 results. 2. PsycINFO; (neurocognitive adj3 remediation).ti,ab; 19 results. 3. PsycINFO; (cognitive adj3 training).ti,ab; 2721 results. 4. PsycINFO; (cognitive adj3 enhancement).ti,ab; 623 results. 5. PsycINFO; (cognitive adj3 rehabilitation).ti,ab; 1277 results. 6. PsycINFO; COGNITIVE REHABILITATION/; 1700 results. 7. PsycINFO; 1 OR 2 OR 3 OR 4 OR 5 OR 6; 5633 results. 8. PsycINFO; SCHIZOPHRENIA/; 67054 results. 9. PsycINFO; PSYCHOSIS/; 18802 results. 10. PsycINFO; (schizo* OR psychosis OR psychotic).ti,ab; 127603 results. 11. PsycINFO; 8 OR 9 OR 10; 130868 results. 12. PsycINFO; 7 AND 11; 779 results. 13. PsycINFO; 12 [Limit to: Publication Year 2010-2014]; 285 results. 14. PsycINFO; CLINICAL TRIALS/; 7131 results. 15. PsycINFO; random*.ti,ab; 124276 results. 16. PsycINFO; groups*.ti,ab; 355206 results. 17. PsycINFO; (doubl* adj3 blind*).ti,ab; 17822 results. 18. PsycINFO; (singl* adj3 blind*).ti,ab; 1560 results. 19. PsycINFO; EXPERIMENTAL DESIGN/; 8850 results. 20. PsycINFO; controlled.ti,ab; 77389 results. 21. PsycINFO; (clinical adj3 study).ti,ab; 7612 results. 22. PsycINFO; trial.ti,ab; 65442 results. 23. PsycINFO; "treatment outcome clinical trial".md; 25317 results. 24. PsycINFO; 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23; 548838 results. 25. PsycINFO; 13 AND 24 [Limit to: Publication Year 2010-2014]; 130 results.	130	
Embase	28. EMBASE; (cognitive adj3 remediation).ti,ab; 747 results. 29. EMBASE; (neurocognitive adj3 remediation).ti,ab; 21 results.	255	

	30. EMBASE; (cognitive adj3 training).ti,ab; 2272 results. 31. EMBASE; (cognitive adj3 enhancement).ti,ab; 882 results. 32. EMBASE; (cognitive adj3 rehabilitation).ti,ab; 1572 results. 33. EMBASE; SCHIZOPHRENIA/; 128943 results. 34. EMBASE; PSYCHOSIS/; 61976 results. 35. EMBASE; (schizo* OR psychosis OR psychotic).ti,ab; 161849 results. 36. EMBASE; 33 OR 34 OR 35; 212028 results. 37. EMBASE; 28 OR 29 OR 30 OR 31 OR 32; 5030 results. 38. EMBASE; 36 AND 37; 1088 results. 39. EMBASE; 38 [Limit to: Publication Year 2010-Current]; 584 results. 40. EMBASE; random*.tw; 857492 results. 41. EMBASE; factorial*.tw; 22008 results. 42. EMBASE; placebo*.tw; 197236 results. 43. EMBASE; (crossover* OR cross-over*).tw; 68527 results. 44. EMBASE; (doubl* adj3 blind*).tw; 141884 results. 45. EMBASE; (singl* adj3 blind*).tw; 16333 results. 46. EMBASE; assign*.tw; 234352 results. 47. EMBASE; allocat*.tw; 80659 results. 48. EMBASE; volunteer*.tw; 174833 results. 49. EMBASE; CROSSOVER PROCEDURE/; 38971 results. 50. EMBASE; DOUBLE-BLIND PROCEDURE/; 118651 results. 51. EMBASE; SINGLE-BLIND PROCEDURE/; 18506 results. 52. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 360008 results. 53. EMBASE; 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52; 1386318 results. 54. EMBASE; 39 AND 53 [Limit to: Publication Year 2010-Current]; 255 results.		
Medline	55. MEDLINE; (cognitive adj3 remediation).ti,ab; 483 results. 56. MEDLINE; (neurocognitive adj3 remediation).ti,ab; 15 results. 57. MEDLINE; (cognitive adj3 training).ti,ab; 1671 results.	136	

	58. MEDLINE; (cognitive adj3 enhancement).ti,ab; 760 results. 59. MEDLINE; (cognitive adj3 rehabilitation).ti,ab; 1008 results. 60. MEDLINE; 55 OR 56 OR 57 OR 58 OR 59; 3634 results. 61. MEDLINE; SCHIZOPHRENIA/; 83382 results. 62. MEDLINE; PSYCHOSIS/; 32221 results. 63. MEDLINE; (schizo* OR psychosis OR psychotic).ti,ab; 133753 results. 64. MEDLINE; 61 OR 62 OR 63; 162038 results. 65. MEDLINE; 60 AND 64; 703 results. 66. MEDLINE; 65 [Limit to: Publication Year 2010-Current]; 326 results. 67. MEDLINE; "randomized controlled trial".pt; 390641 results. 68. MEDLINE; "controlled clinical trial".pt; 89952 results. 69. MEDLINE; placebo.ab; 164006 results. 70. MEDLINE; random*.ab; 721173 results. 71. MEDLINE; trial.ti; 132129 results. 72. MEDLINE; CLINICAL TRIALS AS TOPIC/; 175506 results. 73. MEDLINE; 67 OR 68 OR 69 OR 70 OR 71 OR 72; 1107419 results. 74. MEDLINE; exp ANIMALS/ NOT HUMANS/; 4062541 results. 75. MEDLINE; 73 NOT 74; 1013451 results. 76. MEDLINE; 66 AND 75 [Limit to: Publication Year 2010-Current]; 136 results.		
Summary	NA	NA	

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