Table DS1 Summary of measures.

#	Domain	Assessment
1	Composite Neurocognitive function	Derived by averaging effect sizes of all reported cognitive outcomes
2	Overall neurocognitive function	Brief Assessment Of Cognition In Schizophrenia (BACS), composite Score Clinical Antipsychotic Trials Of Intervention Effectiveness (CATIE) Neurocognitive Battery, composite Score A composite cognitive score as the mean of all standardized domain Repeatable Battery For The Assessment Of Neuropsychological Status (RBANS), composite Score
3	Attention / Vigilance	Continuous Performance Task (CPT) Sum correct, AX-CPT Hit RT, CPT False Alarm RT, IP-CPT Hit RT, IP-CPT False Alarm RT, IP CPT Random Error RT, CPT A', CPT-IP 4 digit d', accuracy Distractibility Version Of The Gordon Diagnostic System (GDS), attention/vigilance The Measurement And Treatment Research To Improve Cognition In Schizophrenia (MATRICS)-attention/vigilance Stroop Test, color Trails A, time Wechsler Adult Intelligence Scale- III (WAIS-III)-Digit Span Forward, Letter Number Span (without reordering) # correct age-scaled score? Weschler Memory Scale-Revised (WMS-R)-Digit Span Forward, BACS, digit sequencing
4	Verbal learning and memory	BACS-List Learning Test, total California Verbal Learning Test (CVLT)-List A immediate free recall trials 1-5, total score Computerized Neurocognitive Scanning-verbal memory Hopkins Verbal Learning Test -Revised (HVLT-R), delayed recall, immediate recall, total # of words recalled in three trials MATRICS (The Measurement And Treatment Research To Improve Cognition In Schizophrenia)-verbal learning Randt Memory Test-5-Item Acquisition Rey Auditory Verbal Learning Test (RAVLT), immediate recall, delayed recall Rey discrimination index Weschler Memory Scale-Revised (WMS-R), composite, logical memory I (immediate), logical memory II (delayed) RBANS, immediate memory (list learning and story learning)
5	Verbal working memory	Auditory Consonant Trigram total correct? Letter Number Test (with reorder), total correct BACS-Number Sequencing Digit Span Distraction Test (DSPT)-Non-Distraction Wechsler Adult Intelligence Scale, Digit Span Backward N-back, letters
6	Spatial learning and memory	Brief Visuospatial Memory Test-Revised Computerized Neurocognitive Scanning-Spatial Memory Object Matching Memory Test (OMMT)-Percent Performance Errors Rey Complex Figure Test (RCFT)-immediate and delayed recall Rey/Taylor Figure (immediate, delayed?) Weschler Memory Scale-Revised (WMS-R), Spatial Span, Visual Reproduction 1 and 2 WMS-Faces immediate Cambridge Automated Neuropsychological Test Battery (CANTAB)-Delayed Matching to Sample (DMS), Pattern Recognition Memory (PRM)
7	Spatial working memory	Cogtest Battery- Object Working Memory Test (OWM)-Delayed 4S total correct Oculomotor Delayed Response Test, 2-Second Delay Simple Spatial Working Memory Test, 15 Sec Delay Visuospatial Working Memory Test (VWMT), Delay 5-second distance, Standardized Difference Between No-Delay Trials And All Delay Trials CANTAB-Span length of Spatial Span (SSP)
8	Reasoning and problem-solving	BACS-Tower Of London Test Computerized Neurocognitive Scanning-Abstraction MATRICS-NAB Mazes, time Stroop Test-Interference time Tower Of Toronto Puzzle Test (TOT), moves Trails B, time Wisconsin Card Sorting Test (WCST)-# categories, % preservative errors Wechsler Intelligence Scale For Children-Third Edition (WISC-III)-Mazes CANTAB-Stocking of Cambridge (SOC)

Table DS1 Summary of measures (Cont'd)

#	Domain	Assessment
9	Speed of processing	BACS-Symbol Coding, Token motor, Verbal fluency
		Controlled Oral Word Association Test (COWAT)-Average # Of FAS Words, total
		Grooved Pegboard Test-Average Pegs
		Letter Number Fluency
		MATRICS-BACS Symbol Coding; Trail A; Category Fluency: Animal Naming
		Verbal Fluency Test (VFT)
		Verbal Productivity
		Wechsler Adult Intelligence Scale-Digit Symbol Substitution Test, Symbol Search
		Finger tapping - Dominan, Nondominant
		CANTAB- Matching to Sample Visual Search (MTS)
10	Social cognition	MATRICS-Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT™): Managing Emotions
		Penn Emotional Acuity Test (PEAT 40)
11	Overall psychiatric symptoms	Brief Psychiatric Symptom Rating (BPRS), total
		Clinical Global Impression(CGI), total
		CGI, Severity
		Positive and Negative Syndrome Scale (PANSS), Total
12	Positive symptoms	Brief Psychiatric Symptom Rating (BPRS), Positive Symptoms
		PANSS, Positive Symptoms
		Scale for the Assessment of Positive Symptoms (SAPS), total
13	Negative symptoms	BPRS, Negative Symptoms
		PANSS, Negative Symptoms
		Scale for the Assessment of Negative Symptoms (SANS), total
14	Depression	Calgary Depression Scale For Schizophrenia (CDSS)
		Hamilton Rating Scale for Depression (HAM-D)
15	Overall functioning	Global Assessment of Function (GAF)
		Personal And Social Performance Scale (PSP), total
		Specific Level Of Function Scale (SLOF), Interpersonal Relationships
		The Quality Of Life Scale (Qol)
16	Excluded	Boston Naming Test (BNT)
		RBANS, Attention, language, visuo/spatial construction, verbal comprehension
		BPRS, Anxiety/Depression, Hostility
		CGI, Global Improvement
		Computerized neurocognitive scanning-Attention, Spatial abilities
		Unirhinal Olfactory Acuity test (UOA)
		Wechsler Adult Intelligence Scale- Block Design
		MATRICS-Working memory (Wechsler Memory Scale 3rd Ed. (WMS-III): Spatial Span; Letter-Number Span)
		PANSS-General Psychopathology Symptoms
		Woodcock-Johnson
		Automated Neuropsychological Assessment Metrics (ANAM)
		Preparing to overcome prepotency task

Table DS2 Summary of characteristics, effect-sizes and conclusions from studies of adjunctive pharmacotherapy included in the meta-analysis (*N*=26).

Author	Cognitive Enhancing Meds	Pharmacologic Targets	Maximum Dose of Cog Enhancing Medication	Trial Period (Week)	Medication Adherence Monitor	N (Tx, Ctrl)	Age (Tx, Ctl)	Antipsychotic Medication
Akhondzadeh et al. (2008)[44]	donepezil	AChEI	10	12	Yes	(15, 15)	(32.3, 33.9)	Risperidone (5mg for treatment; 5mg for placebo)
Fagerlund et al. (2007) [9]	donepezil	AChEI	10	16	Not Specified	(7, 4)	(33.2, 35.0)	Zyprasidone (142.9 for treatment; 115 for placebo)
Freudenreich. (2005) [45]	donepezil	AChEI	10	8	Yes	(15, 15)	(48.7, 48.7)	Mix of atypical and typical
Friedman et al. (2002)[10]	donepezil	AChEI	10	12	Not Specified	(18, 18)	(50.3, 48.8)	Risperidone (5.9 for treatment; 6.4 for placebo)
Keefe et al. (2008)[11]	donepezil	AChEI	10	12	Yes	(121, 124)	(40.9, 39.7)	Any second generation antipsychotics
Kohler et al. (2007)[12]	donepezil	AChEI	10	16	Not Specified	(11, 11)	(31.7, 30.0)	Atypical (Olanzapine equivalents=16.5mg, SD±9.5)
Lee et al. (2007) [16]	donepezil	AChEI	5	12	Not Specified	(12, 12)	(42.2, 44.2)	Haloperidol up to 30 mg (14.4 for treatment; 17 for placebo)
Buchanan et al. (2008)[14]	galantamine	AChEI	24	12	Yes	(42, 44)	(49.9, 49.5)	A second generation antipsychotic other than Clozapine or a low-dose conventional antipsychotics
Lindenmayer et al. (2011)[46]	galantamine	AChEI	24	24	Yes	(15, 17)	(41.9, 38.5)	Risperidone (long-acting injectable) (40.79 for treatment; 38.16 for placebo)
Dyer et al. (2008)[17]	galantamine	AChEI	16	8	Yes	(10, 10)	(44.3, 50.5)	Clozapine, Risperdone, Aripiprazole, Olanzapine, Siprasidone, Quetiapine
Lee et al. (2007)[47]	galantamine	AChEI	16	12	Not Specified	(12, 12)	(39.5, 41.5)	Conventional antipsychotics (i.e., chlorpromazine equivalent dose of 1390mg/day)
Schbert et al. (2006) [48]	galantamine	AChEI	24	8	Not Specified	(8, 8)	(48.3, 46.8)	Risperidone (average dose=5.75±1.3 for treatment; 5.25±1.0 for control)
Sharma et al. (2006)[13]	rivastigmine	AChEI	6	24	Not Specified	(11, 10)	(42.6, 46.8)	Mixture of Risperidone, Olanzapine, Quetiapine

TableDS2 Summary of characteristics, effect-sizes and conclusions from studies of adjunctive pharmacotherapy included in the meta-analysis (*N*=26) (Cont'd)

Other Medication	Period Stabilized (Week)	Screening Process	Smokers (1=yes; 2=no; 3=not reported)	ES for Averaged Neurocognition	Main findings
Anticholingergis, sedating antihistaminics, antidepressants, mood stabilizers or a second antipsychotics were not allowed for the duration of this study.	8	More than 20 on MMSE	3	0.03	Greater improvement in the negative symptoms. No differences on any neurocognitive assessments at week 12.
The following medications were not allowed during the study: anticholinergics, tricyclic antidepressants, antipsychotics other than ziprasidone, and mood stabilizers. However, selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines were allowed throughout the study (benzodiazepines were allowed only after cognitive assessments).	8	No	1	0.00	No treatment effects on cognition
Subjects taking antipsychotics that are considered strongly anticholinergic were excluded (e.g., clozapine and low-potency conventional antipsychotics); subjects could not be on ancillary medications with anticholinergic properties (e.g., benztropine or trihexyphenidyl).	-	More than 20 on MMSE	1	-0.21	No treatment effects on residual symptoms and cognitive problems
Not allowed for the duration of the study: anticholinergics, sedating antihistaminics, antidepressants, mood stabilizers or a second antipsychotic. Benzo use was limited to medium or short-acting preparations and was held for 24 hours before cognitive testing.	4	At least two standard deviation below on the CVLT	1	-0.09	No improvements in any cognitive measure compared with placebo.
No adjunctive anticholinergic medication. Patients on stable doses of selected antidepressants and antiepileptics were permitted. Anxiolytics were excluded. Sedative hypnotics were limited.	-	z-score between -0.5 and -2.5 SD (BACS composite scores)	1	-0.20	Not effective of cognitive impairment. A surprisingly large placebo/practice effect
No antidepressants, mood stabilizers, or benzodiazepines			1	0.52	No treatment effects on any cognitive functions or clinical symptoms
Antiparkinsonian anticholinergics and benzodiazepines were allowed if their doses did not change during the 12 weeks.	12	Between 15 and 24 on the K-MMSE	1	0.61	Improvement on the K-MMSE scores; slight improvement in several cognitive measures; No improvement in psychiatric symptoms
No anticholinergics	-	A total score of 90 or less on the RBANS	1	0.04	No significant treatment effect on the overall composite neurocognition score; Significant treatment effect on the WAIS-III digit symbol and verbal memory measures. In contrast, the subjects taking placebo showed a significant improvement on the GDS distractibility test. No significant between-group differences in motor speed or working memory.
No anticholingergics	24		3	-0.30	No treatment effects on cognitive measures
No anticholinergics, illicit drug, a nicotine containing product, air carbon monoxide (CO)>9, salivary drug screen positive for cotinine, cocaine, THC, ethanol, amphetamine, or benzodiazepines	8		2	-0.11	No treatment effects on cognitive measures
Use of anticholinergics: .667 for treatment; .75 for control; Anti-parkinsonian anticholinergics and benzodiazepines were permitted if the dose did not change during the 12 weeks	12	All of the pts complained of cog deficits	1	0.39	No treatment effects on cognitive measures or state of psychopathology measures.
None	4		1	1.09	Adjunctive treatment with Galantamine improves memory and attention in patients with schizophrenia who are stabilized on Risperidone.
No anticholinergic meds	6	Reading ability of not more than 40 errors on NART; Between 1 and 2 SDs below expected performance on the CVLT	1	0.13	No treatment effects on any cognitive measure. Some cognitive variables showed significant practice effects in both the placebo and Rivastigmine groups. No effects were noted in symptoms.

Table DS2 Summary of characteristics, effect-sizes and conclusions from studies of adjunctive pharmacotherapy included in the meta-analysis (*N*=26) (Cont'd)

Author	Cognitive Enhancing Meds	Pharmacologic Targets	Maximum Dose of Cog Enhancing Medication	Trial Period (Week)	Medication Adherence Monitor	N (Tx, Ctrl)	Age (Tx, Ctl)	Antipsychotic Medication
Buchanan et al. (2007)[21]	D-cycloserine	GLU agonist	50	16	Yes	(40, 38)	(44.4, 43.4)	Mixed (conventional and atypical)
Tsai et al. (1998)[20]	D-serine	GLU agonist	30	6	Not Specified	(14, 15)	(33.9, 31.7)	Mix of conventional and atypical (chlorpromazine equvalent=635mg±546 for D-serine; 1012mg±725 for placebo)
Tsai et al. (1999)[22]	D-serine	GLU agonist	30	6	Not Specified	(10, 10)	(42.6, 39.5)	Clozapine (363mg/day for D-Serine group; 314 mg/day for Placebo group)
Goff et al. (1999)[49]	D-cycloerine	GLU agonist	50	8	Yes	(15, 22)	(46.8, 41.2)	Conventional antipsychotics (A variety of oral conventional neuroleptics at different dose)
Goff et al. (2008)[50]	D-cycloserine	GLU agonist	50mg (once weekly)	8	Not Specified	(19, 19)	(50.1, 48)	Aripiprazole, Risperidone, Ziprasidone, Olanzapine, Quetiapine, Fluphenazine, Haloperidol, Loxitane
Goff et al. (2001)[51]	CX516	GLU agonist	900, 3600	4	Not Specified	(12, 6)	Not Specified	Clozapine
Goff et al. (2008)[52]	CX516	GLU agonist	2700	4	Not Specified	(51, 54)	(42, 43.7)	Clozapine (432 for treatment, 426 for placebo), Olanzapine (22.4 for treatment, 19.3 for placebo), Risperidone (4 for treatment, 4.1 for placebo)
Piskulic et al. (2009)[27]	buspirone	Serotonergic agonist	30	6	Yes	(9, 9)	(43.4, 37.2)	Clozapine, Risperidone, Olanzapine, Quetiapine And Amisulpride
Sumiyoshi et al. (2007)[25]	buspirone	Serotonergic agonist	30	24	Yes	(30, 29)	(40.5, 39.7)	Risperidone, Olanzapine, Ziprasidone, Ziprasidone (Risperidone equivalent dose=4.2±1.9 for Buspirone; 3.9±2.0 for placebo)
Sumiyoshi et al. (2001)[26]	tandospirone	Serotonergic agonist	30	6	Not Specified	(15, 11)	(27.8, 31.8)	Typical (Haloperidol, Sulpride, Pimoizide; Neuroletpic dose (mg/day)=250±245 for treatment; 230±215 for placebo)
Sumiyoshi et al (2001)[53]	tandospirone	Serotonergic agonist	30	4	Not Specified	(11, 11)	(28.9, 28.9)	Typical (Haloperidol- 6.9mg, Biperiden-4.0mg for treatment; Haloperidol-5.1mg, Biperiden-3.5mg)
Shiina et al (2010)[54]	tropisetron	Serotonergic agonist	10	8	Not Specified	(16.17)	(34.9, 35.2)	Risperidone
Poyurovsky et al. (2003)[28]	mianserin	Serotonergic agonist	15	4	Not Specified	(11, 13)	(42.5, 45.5)	Conventional antipsychotics (i.e. Haloperidol 10-40mg, cholorpromazine 300-600mg, or perphenazine 16-32 mg)

Table DS2 Summary of characteristics, effect-sizes and conclusions from studies of adjunctive pharmacotherapy included in the meta-analysis (*N*=26) (Cont'd)

Other Medication	Stabilized (Week)	Screening Process	Smokers	ES	Main findings
Subjects were also allowed to remain on concomitant anticholinergic, beta-blocker, mood stabilizer, antidepressant, antianxiety, or anticonvulsant medication regimens	-	No	3	-0.21	No treatment effects on negative symptoms or cognitive impairments.
Not specified	12	SANS >=40 CGI>=4	3	0.45	Improvements on positive, negative, and cognitive symptoms as well as some performance in WCST.
Not specified	6		3	-0.15	No improvement with D-serine, nor did their symptoms worsen.
All other medications remained unchanged; Participants were excluded who were taking an anticholinergic medication or who reported use of an illicit drug or a nicotinecontaining product in the past 3 months or who had expired air carbon monoxide (CO) N9 ppm or salivary drug screen positive for cotinine, cocaine, THC, ethanol, amphetamine, or benzodiazepines at screening.	16		3	-0.10	No treatment effects on any cognitive test between groups or in changes in any other clinical measure. The mean reduction in negative symptoms with D-Cycloserine (23%) was significantly greater than with placebo (7%) as calculated by slopes representing Scale for the Assessment of Negative Symptoms (SANS) total scores.
Not specified	4	Patients unable to complete the cognitive battery at baseline were dropped from study	3	0.38	D-Cycloserine improved SANS total scores compared to placebo at week 8. Cognitive performance did not improve with D-Cycloserine at 8 weeks. Delayed thematic recall on the Logical Memory Test was improved with the first dose of D-Cycloserine compared to placebo. Performance on immediate thematic recall and item recall on the Logical Memory Test did not differ between treatments.
Not reported	24		3	0.55	CX516 was associated with moderate to large, between-group effect sizes compared with placebo, representing improvement in measures of attention and memory.
Concomitant medications were allowed, except for benzodiazepines 8 h before cognitive testing	24		3	0.00	No group differences on the composite cognitive score, or on any cognitive test at weeks 4 or 8. The placebo group improved more on the PANSS total score than the CX516 group; no other clinical rating differed between treatment groups.
All other medications remained unchanged	8		3	-0.41	No treatment effects on either cognitive function measures or symptom ratings.
Subjects were excluded if they 1) were pregnant or lactating, 2) were taking a mood stabilizer, antidepressants, anticholinergic or anxiolytic drugs; All other medications remained unchanged	12		3	0.11	No interaction effects were noted for other domains of cognition. Scores on the Brief Psychiatric Rating Scale (Total, Positive) were improved during treatment with Buspirone but not placebo, but the effects did not reach statistical significance.
All other medications remained unchanged	12		3	0.39	Both cognitive measures improved significantly in the patients who received Tandospirone; subjects who did not received Tandospirone showed no change. There was no significant change in psychopathology ratings in either group.
Not reported	-	Not reported	3	0.05	A significant time by group (patients with or without tandospirone) effect for the Verbal-, but not the Visual Memory composite scores of the WMS-R test.
Benzodiazepine, anticholinergics, lithium, milnacipran, trazodone, alproic acid, carbamazepine	4	Not reported	1	-0.17	Performance on the eight domains of the CANTAB did not differ between tropisetron group and placebo group.
Benzodiazpines, Anticholinergic agent for EPS, or mood stabilizer	24	Patients unable to complete the cognitive battery at baseline were dropped from study	3	0.36	The Mianserin group overperformed the placebo group on selective ANAM memory/learning tests, reflected in moderate-to-high effect size values. No between-group differences were revealed in WCST and clinical ratings.

Table DS3 Summary of medication adherence check, funding sources and regions from studies of adjunctive pharmacotherapy included in the meta-analysis (*N*=26)

#	Cognitive Enhancing Meds	Author	Year	Study Medication Adherence Check	Funding Sources	Types of Fund Sources (1=pharm, 2=non-pharm, 3=unknown)	Region
1	donepezil	Akhondzadeh et al[44]	2008	Surplus tablets were counted each study visit	Tehran University of Medical Sciences	2	Iran
2	donepezil	Fagerlund et al[9]	2007	NR	An unrestricted grant from Pfizer	1	Denmark
3	donepezil	Freudenreich[45]	2005	Surplus capsules were counted each study visit	Pfizer, NARSAD, CRTF, NIHM	1	USA
4	donepezil	Friedman et al[10]	2002	NR	Janssen Research Foundation & the Clinical Trials Unit, VA VISN 3 MIRECC	1	USA
5	donepezil	Keefe et al[11]	2008	Safety, tolerability, and compliance evaluations included all medication use, adverse events (AEs), study drug dispensing, and medication compliance.	Eisai Inc. & Pfizer inc.	1	USA
6	donepezil	Kohler et al[12]	2010	NR	N/A	3	USA
7	donepezil	Lee et al[16]	2007	NR	Inje University	2	South Korea
8	galantamine	Buchanan et al[14]	2008	Assessed by weekly pill count and medication review.	VA Capitol Network MIRECC, Education, and Clinical Center; Stanley; NIMH; Doubleblind medications were provided by Ortho-McNeil Neurologics	2	USA
9	galantamine	Lindenmayer et al[46]	2011	Patients were excluded if they were deemed treatment resistant by the investigator	Janssen	1	USA
10	galantamine	Dyer et al[17]	2008	Medication compliance was assessed weekly by self-report and pill counts.	NIDA, NIMH	2	USA
11	galantamine	Lee et al[47]	2007	NR	n/a	3	South Korea
12	galantamine	Schbert et al[48]	2006	NR	VA Office of Academic Affiliations Post-Residency Fellowship Program;	2	USA
13	rivastigmine	Sharma et al[13]	2006	NR	Stanley	2	UK
14	D-cycloserine	Buchanan et al[21]	2007	Assessed by a pill count and medication review at the biweekly visits	Treatment of Negative Symptoms and Cognitive Impairments grants; NIMH; VA Capitol Network (VISN 5) MIRECC.	2	USA & Israel
15	D-serine	Tsai et al[20]	1998	NR	NARSAD, Stanley Peter and Elizabeth C. Tower Foundation	2	Taiwan
16	D-serine	Tsai et al[22]	1999	NR	NARSAD, Stanley	2	Taiwan
17	D-cycloserine	Goff et al[49]	1999	Assessed weekly by self-report and pill counts.	NIMH	2	USA
18	D-cycloserine	Goff et al[50]	2008	NR	NIH, Stanley	2	USA
19	CX516	Goff et al[51]	2001	NR	Cortex Pharmaceuticals	1	USA
20	CX516	Goff et al[52]	2008	NR	NIMH	2	USA
21	buspirone	Piskulic et al[27]	2009	Monitored by pill count	Stanley	2	Australia
22	buspirone	Sumiyoshi et al[25]	2007	Assessed by weekly pill count.	NARSAD, Pharmacopsychiatry research grant from the Mitsubishi pharma research foundation, some japan research grants	1	USA
23	tandospirone	Sumiyoshi et al[26]	2001a	NR	Japan Research Foundation for Clinical Pharmacology, NARSD	2	Japan
24	tandospirone	Sumiyoshi et al[53]	2001b	NR	Warren foundation, Japanese research foundation	2	Japan
25	tropisetron	Shiina et al[54]	2010	NR	Stanley	2	Japan
26	mianserin	Poyurovsky et al[28]	2003	NR	Not reported	3	Israel