Data supplement to Gregory et al. Treatment of depression in schizophrenia: systematic review and meta-analysis. Br J Psychiatry doi: 10.1192/bjp.bp.116.190520

Table DS1 Included studies

Class	Author, Year	1º Outcome	Participants	Antidepressant	Dose	Antipsychotic	N	Duration (weeks)	Outcomes	Recovery Criteria	Result
SSRI	(Hinkelmann et al., 2013)	Negative symptoms	DSM-IV schizophrenia Predominantly negative symptoms	Citalopram and Reboxetine	20-40mg C, 4-8 mg R	Various FGAs and SGAs	58	4	PANSS, HAM-D, CGI	N/A	Improvement in citalopram group No change with Reboxetine
	(Kasckow et al., 2001)	Depression (not explicitly stated)	DSM-IV schizophrenia HRSD>12	Citalopram	20-40mg	Various FGAs and SGAs	19	10	PANSS, HRSD, CGI, MMSE	N/A	Significantly greater improvement in citalopram group
	(Taiminen et al., 1997)	Positive and negative symptoms	DSM-III schizophrenia Stable	Citalopram	40mg	Various FGAs and SGAs	75	12	PANSS, HRSD	N/A	Citalopram group improved more than placebo in depressive domain of PANSS
	(Zisook et al., 2009)	Depression	DSM-IV schizophrenia, schizoaffective Subsyndromal depression (HRSD>8, 2/4 DSM-IV MDE)	Citalopram	20-40mg	Various FGAs and SGAs	212	12	PANSS, HRSD, CGI, CDSS, QLS	>50% improvement in HRSD	Citalopram significantly more effective than placebo for depressive symptoms
	(Arango et al., 2000)	N/A	DSM-III schizophrenia	Fluoxetine	20mg	Various FGAs and SGAs	32	8	BPRS HRSD, SANS, MIMS	N/A	Fluoxetine not superior to placebo
	(Buchanan et al., 1996)	Positive and negative symptoms	DSM III schizophrenia or schizoaffective disorder Treatment resistant	Fluoxetine	20-80mg	Clozapine	34	8	BPRS, SANS, HRSD	N/A	No group differences on any measures
	(Niitsu et al., 2012)	Cognitive impairment	DSM-IV schizophrenia, Chronic, stable	Fluvoxamine	50-100mg	Atypical antipsychotics	48	8	PANSS, SANS, QLS, MADRS, CANTAB	N/A	No significant depressive changes with fluvoxamine

Class	Author, Year	1º Outcome	Participants	Antidepressant	Dose	Antipsychotic	N	Duration (weeks)	Outcomes	Recovery Criteria	Result
	(Addington et al., 2002a)	Depression	DSM-IV schizophrenia, schizoaffective DSM-IV diagnosis MDE	Sertraline	50-100mg	Various FGAs and SGAs	48	6	CDSS, DSM-IV-MDE, HRSD, PANSS	≥50% reduction in CDSS score	No difference between groups for depressive symptoms
	(Izakova et al., 2009)	Depression	ICD-10 and DSM-IV Schizoaffective disorder, depressed type. CDSS>5 First episode and recurrently ill	Sertraline	50mg + (mean wk 12= 133.82)	Risperidone in control, haloperidol in intervention	54	12	PANSS, CDSS, CGI	N/A	Comparable effect for both treatment regimes in terms of depressive symptoms
	(Mulholland et al., 2003)	Depression	DSM III schizophrenia, Depressed >15 BDI	Sertraline	50-100mg	Various FGAs and SGAs	26	8	HRSD, BPRS, CGI	CGI dichotomous outcome of 'minimal' or 'better' improvement	No difference between groups on ITT analysis
	(Omranifard et al., 2012)	Depression	DSM-IV schizophrenia, subsyndromal Depressive symptoms	Sertraline	50-200mg	FGAs and SGAs	60	12	CDSS, GAF	N/A	Significantly greater improvement in sertraline group
TCA	(Prusoff et al., 1979)	Depression (Not explicitly stated)	DSM-III-R schizophrenia Raskin Depression>7	Amitriptyline	100-200mg	Perphenazine	40	24	BPRS, HRSD, Raskin depression	Global psychiatric status physician rated 'moderate improvement' at 6 months	Advantage of amitriptyline after 4 months.
	(Hogarty et al., 1995)	Depression (Not explicitly stated)	Schizophrenia: RDC Raskin depression>7 for 3 months prior	Desipramine	50-150mg	Fluphenazine decanoate	33	12	CGI, BPRS, BDI	CGI score showed 'much improvement'	Significant benefit of antidepressant using BDI, BPRS

Class	Author, Year	1º Outcome	Participants	Antidepressant	Dose	Antipsychotic	N	Duration (weeks)	Outcomes	Recovery Criteria	Result
	(Kramer et al., 1989)	Depression (Not explicitly stated)	RDC schizophrenia, schizoaffective RDC MDE, HRSD>17	Desipramine, Amitriptyline	Both 3.5mg/kg /day	Haloperidol	58	4	HRSD, BPRS	N/A	Antidepressant groups did not differ from placebo in depressive symptoms
	(Becker, 1983)	Depression (Not explicitly stated)	DSM II schizophrenia RDC for depressive syndrome plus HRSD 3 or 4 (depressed) or 3 or 4 (anergic)	Imipramine	75-250mg	Thioxene in placebo, chlorpromazine in placebo	52	4	BPRS, HRSD, CGI	N/A	No difference between groups for any factor.
	(Siris et al., 2000)	Depression (Not explicitly stated)	Schizophrenia or schizoaffective (RDC) DSM-IV post psychotic depression HRSD>12	Imipramine	50-200mg	Fluphenazine decanoate	72	6	SADS-extracted HRSD score, CGI, GAS	CGI 'much improved' or 'very much improved'	Favoured the imipramine group
	(Johnson, 1981)	Depression (Not explicitly stated)	Positive Feighner symptoms Depressed BDI >15	Nortriptiline	25-150 mg	Fluphenazine or flupenthixol decanoate	50	5	HRSD, BPRS	≥33% reduction in HRSD score	No difference between groups in depression alleviation
Receptor blocker	(Shiloh et al., 2002)	N/A "Efficacy"	DSM-IV schizophrenia Treatment resistant	Mianserin	30mg	FGA	18	6	BPRS, SAPS, SANS, HRSD	N/A	Decreases in HRSD did not differ between groups
	(Berk et al., 2001)	Negative symptoms	DSM-IV schizophrenia First episode and recurrently ill	Mirtazapine	30mg	Haloperidol	30	6	PANSS, CGI, HRSD	N/A	No between group effects for depressive symptoms at 6 weeks
	(Berk et al., 2009)	Positive and negative symptoms	Diagnosis of schizophrenia on mini interview	Mirtazapine	30mg	SGAs	40	6	PANSS, HRSD, CDSS	N/A	No significant difference between groups
	(Terevnikov et al., 2011)	Original trial PANSS	DSM-IV TR schizophrenia,	Mirtazapine	30mg	FGAs	41	6 double-blind, 6	CDSS, PANSS, CGI	N/A	No significant difference in favour of

Class	Author, Year	1º Outcome	Participants	Antidepressant	Dose	Antipsychotic	N	Duration (weeks)	Outcomes	Recovery Criteria	Result
		Open-label extension-depression	schizoaffective disorder					open extension			mirtazapine over placebo
SNRI	(Mico et al., 2011)	N/A "Efficacy on symptoms, cognitive functioning"	DSM-IV schizophrenia BPRS>25	Duloxetine	60mg	Clozapine	40	16	BPRS, CDSS, PANSS, WCST, verbal fluency.	N/A	Duloxetine significantly reduced CDSS. No sig changes in placebo group
	(Kurland and Nagaraju, 1981)	Depression (Not explicitly stated)	Diagnosed schizophrenic HRSD>18	Viloxazine	150-300 mg	Haloperidol and chlorpromazine	28	4	BPRS, HRSD	N/A	No difference between placebo and viloxazine
MAO-B inhibitor	(Bodkin et al., 2005)	Negative Symptoms (Not explicitly stated)	DSM-III schizophrenia SANS>12	Selegelline	10mg	FGAs and SGAs	67	12	SANS, BPRS, HRSD, CGI	N/A	Non-significant improvement in depressive symptoms with selegelline
NDRI	(Dufresne et al., 1988)	Depression (Not explicitly stated)	DSM-III schizophrenia DSM-III MDE, HRSD>18	Bruproprion	150-750mg	Thioxene	38	10	BPRS, CGI, HRSD	N/A	Antidepressant less effective for depression than antipsychotic alone
SARI	(Singh, Apr 1978)	Depression (Not explicitly stated)	Feighner's criteria for schizophrenia HRSD>18	Trazodone	50-100mg	Phenothiaxine	60	6	BPRS, HRSD, CGI	CGI 'improved'	Trazodone greater than placebo in improving depressive symptomatology

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Kramer, M. S., Vogel, W. H., DiJohnson, C., Dewey, D. A., Sheves, P., Cavicchia, S., ... & Kimes, I. (1989). Antidepressants in 'depressed' schizophrenic inpatients: a controlled trial. *Archives of General Psychiatry*, *46*(10), 922-928.

Shiloh, R., Zemishlany, Z., Aizenberg, D., Valevski, A., Bodinger, L., Munitz, H., & Weizman, A. (2002). Mianserin or placebo as adjuncts to typical antipsychotics in resistant schizophrenia. *International clinical psychopharmacology*, *17*(2), 59-64.

Fig. DS1: Risk of Bias Assessment Summary using Cochrane Risk of Bias Tool

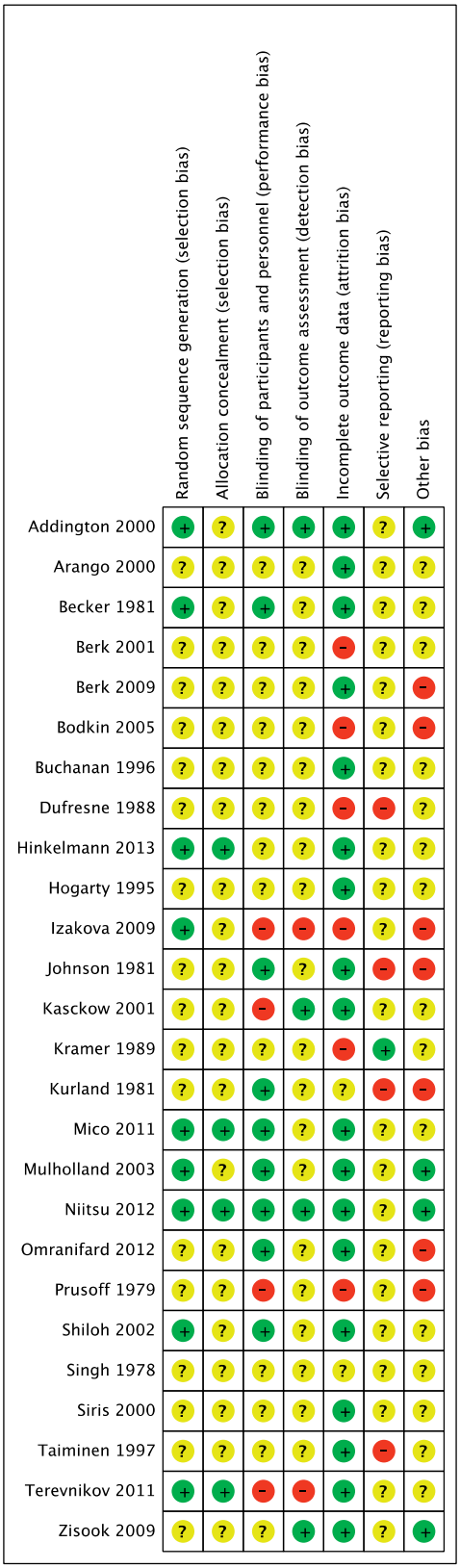


Fig. DS2: Schizophrenia vs mixed schizophrenia and schizoaffective using categorical response/no response end-point

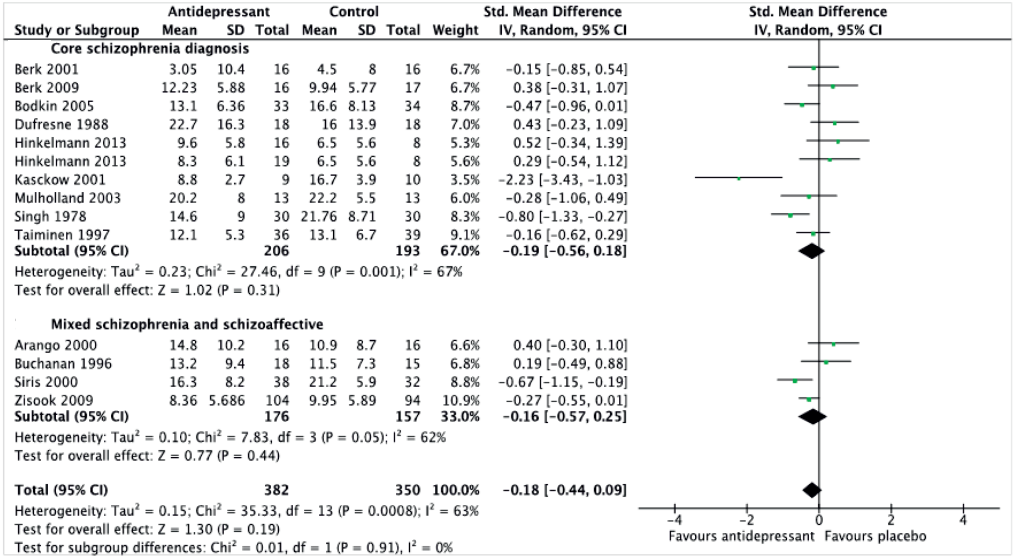
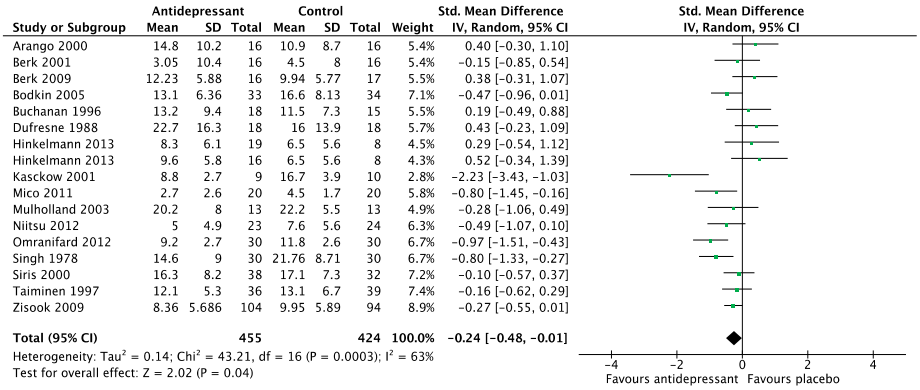


Fig. DS3: Improvement in end point depression score: Studies reporting end-point depression score and standard deviation:



Sensitivity analysis for Improvement in end-point depression score: all anti-depressants: Kasckow 2001 removed

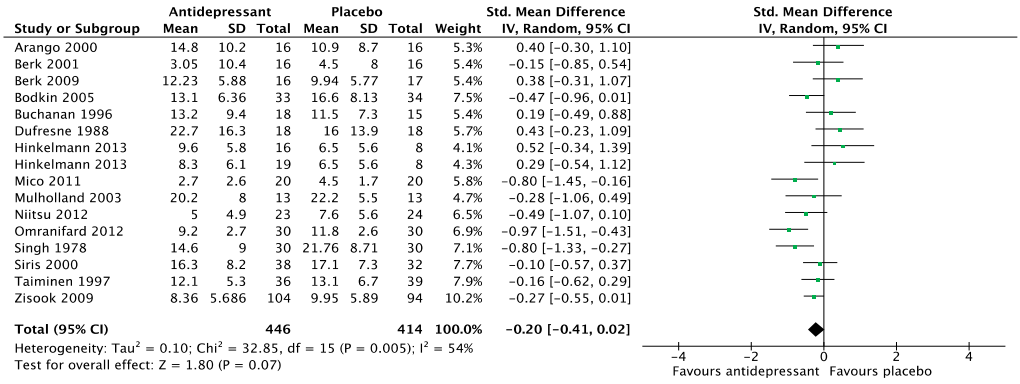


Fig. DS4: short (4-6 weeks) vs long (8-12 weeks) follow up. Studies included if using end-point HRSD and provided means and standard deviation.

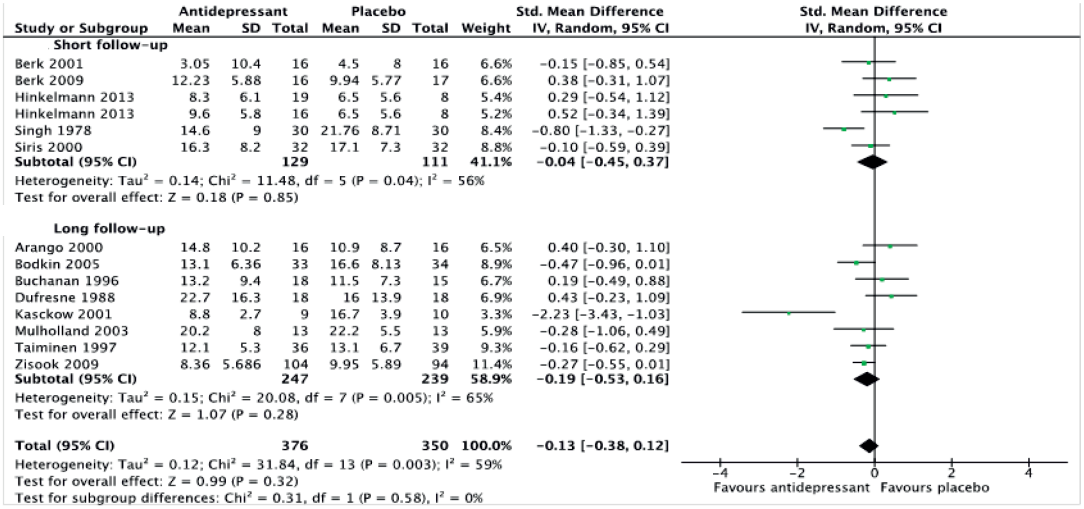


Fig. DS5: Studies reporting on SSRIs using end-point HRSD scores and provided means and standard deviation

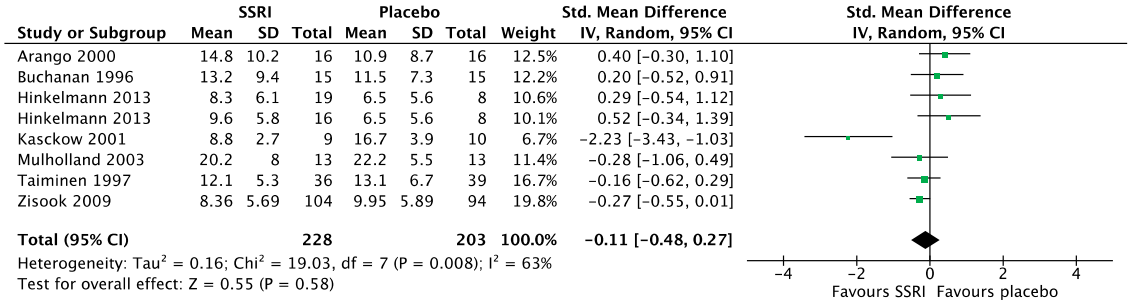


Fig DS6: other antidepressants (Receptor blockers, MAO-Bi, SNRI, NDRI). Studies using end-point HRSD scores and provided means and standard deviation

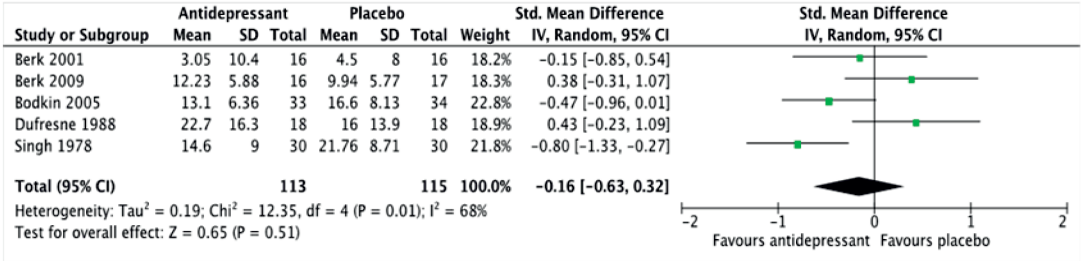


Fig. DS7: Funnel Plot of Included Studies