

Data supplement

Supplemental search strategy term list

- 1 "Schizophrenia" [Mesh]
- 2 Schizophr\* [Title/Abstract]
- 3 Schizoaff\* [Title/Abstract]
- 4 #1 OR #2 OR #3
- 5 "Antipsychotic agents" [Mesh]
- 6 Antipsychotic\* [Title/Abstract]
- 7 #5 OR #6
- 8 "Sultopride" [Supplementary Concept]
- 9 Amisulpride[Title/Abstract]
- 10 "Aripiprazole" [Supplementary Concept]
- 11 Aripiprazole[Title/Abstract]
- 12 "Olanzapine" [Supplementary Concept]
- 13 Olanzapine [Title/Abstract]
- 14 "Quetiapine" [Supplementary Concept]
- 15 Quetiapine [Title/Abstract]
- 16 "9-hydroxy-risperidone" [Supplementary Concept]
- 17 Paliperidone [Title/Abstract]
- 18 "Risperidone" [Mesh]
- 19 Risperidone [Title/Abstract]
- 20 "Ziprasidone" [Supplementary Concept]
- 21 Ziprasidone[Title/Abstract]
- 22 ##8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
- 23 "Chlorpromazine"[Mesh]
- 24 Chlorpromazine [Title/Abstract]
- 25 "Haloperidol"[Mesh]
- 26 Haloperidol[Title/Abstract]
- 27 "Sulpiride" [Mesh]
- 28 Sulpiride[Title/Abstract]
- 29 "Trifluoperazine"[Mesh]
- 30 Trifluoperazine [Title/Abstract]
- 31 #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30
- 32 "Paliperidone palmitate" [Supplementary Concept]
- 33 Paliperidone palmitate[Title/Abstract]
- 34 Risperidone long-acting [Title/Abstract] OR Risperidone depot [Title/abstract]
- 35 #32 OR #33 OR #34
- 36 "Flupenthixol decanoate" [Supplementary Concept]
- 37 Flupenthixol decanoate [Title/Abstract]
- 38 "Fluphenazine depot" [Supplementary Concept]
- 39 "Fluphenazine depot" [Title/Abstract]
- 40 "Haloperidol decanoate" [Supplementary Concept]
- 41 Haloperidol decanoate [Title/Abstract]
- 42 "Pipothiazinepalmitate" [Supplementary Concept]
- 43 Pipothiazinepalmitate[Title/Abstract]

44 *"Clopenthixol acetate ester" [Supplementary Concept]*  
45 *Clopenthixol acetate\*[Title/Abstract]*  
46 *#36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45*  
47 *#7 OR #22 OR #31 OR #35 OR #46*  
48 *#4 AND #47*  
49 *Randomized controlled trial [Publication Type]*  
50 *Controlled clinical trial [Publication Type]*  
51 *Randomized [Title/Abstract]*  
52 *Placebo [Title/Abstract]*  
53 *Randomly [Title/Abstract]*  
54 *"Clinical Trials as Topic" [Mesh:NoExp]*  
55 *Trial [Title]*  
56 *#49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55*  
57 *#48 AND #56*

## Supplemental reference list

1. Arato M, O'Connor R, Meltzer HY, Group ZS. A 1-year, double-blind, placebo-controlled trial of ziprasidone 40, 80 and 160 mg/day in chronic schizophrenia: the Ziprasidone Extended Use in Schizophrenia (ZEUS) study. *International clinical psychopharmacology* 2002; **17**(5): 207-15.
2. Bai YM, Ting Chen T, Chen JY, et al. Equivalent switching dose from oral risperidone to risperidone long-acting injection: a 48-week randomized, prospective, single-blind pharmacokinetic study. *The Journal of clinical psychiatry* 2007; **68**(8): 1218-25.
3. Beasley CM, Jr., Sanger T, Satterlee W, Tollefson G, Tran P, Hamilton S. Olanzapine versus placebo: results of a double-blind, fixed-dose olanzapine trial. *Psychopharmacology* 1996; **124**(1-2): 159-67.
4. Bechelli LPC, Lecco MC, Pontes MC. A double-blind trial of haloperidol decanoate and pipothiazine palmitate in the maintenance treatment of schizophrenics in a public out-patient clinic. *Current Therapeutic Research* 1985;37: 662-71.
5. Breier A, Berg PH, Thakore JH, et al. Olanzapine versus ziprasidone: results of a 28-week double-blind study in patients with schizophrenia. *The American journal of psychiatry* 2005; **162**(10): 1879-87.
6. Cassano GB, Castrogiovanni P, Conti L, Bonollo L. Sulpiride versus haloperidol in schizophrenia: a double-blind comparative trial. *Current therapeutic research, clinical and experimental* 1975; **17**(2): 189-201.
7. Chen EY, Hui CL, Lam MM, et al. Maintenance treatment with quetiapine versus discontinuation after one year of treatment in patients with remitted first episode psychosis: randomised controlled trial. *Bmj* 2010; **341**: c4024.
8. Colonna L, Saleem P, Dondey-Nouvel L, Rein W. Long-term safety and efficacy of amisulpride in subchronic or chronic schizophrenia. Amisulpride Study Group. *International clinical psychopharmacology* 2000; **15**(1): 13-22.
9. Crawford R, Forrest A. Controlled trial of depot fluphenazine in out-patient schizophrenics. *The British journal of psychiatry : the journal of mental science* 1974; **124**(0): 385-91.
10. Crespo-Facorro B, Perez-Iglesias R, Mata I, et al. Relapse prevention and remission attainment in first-episode non-affective psychosis. A randomized, controlled 1-year follow-up comparison of haloperidol, risperidone and olanzapine. *Journal of psychiatric research* 2011; **45**(6): 763-9.
11. Csernansky JG, Mahmoud R, Brenner R, Risperidone USASG. A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. *The New England journal of medicine* 2002; **346**(1): 16-22.
12. de Sena EP, Santos-Jesus R, Miranda-Scippa A, Quarantini Lde C, Oliveira IR. Relapse in patients with schizophrenia: a comparison between risperidone and haloperidol. *Revista brasileira de psiquiatria* 2003; **25**(4): 220-3.
13. Deberdt W, Lipkovich I, Heinloth AN, et al. Double-blind, randomized trial comparing efficacy and safety of continuing olanzapine versus switching to quetiapine in overweight or obese patients with schizophrenia or schizoaffective disorder. *Therapeutics and clinical risk management* 2008; **4**(4): 713-20.
14. Dellva MA, Tran P, Tollefson GD, Wentley AL, Beasley CM, Jr. Standard olanzapine versus placebo and ineffective-dose olanzapine in the maintenance treatment of schizophrenia. *Psychiatric services* 1997; **48**(12): 1571-7.
15. Dencker SJ, Frankenberg K, Malm U, Zell B. A controlled one-year study of pipotiazine palmitate and fluphenazine decanoate in chronic schizophrenic syndromes. Evaluation of results at 6 and 12 months' trial. *Acta psychiatrica Scandinavica Supplementum* 1973; **241**: 101-18.
16. Dencker SJ, Lepp M, Malm U. Clopenthixol and flupenthixol depot preparations in outpatient schizophrenics. I. A one year double-blind study of clopenthixol decanoate and flupenthixol palmitate. *Acta psychiatrica Scandinavica Supplementum* 1980; **279**: 10-28.
17. Dotti A, Bersani G, Rubino IA, Eliseo C. Double-blind trial of fluphenazine decanoate against placebo in ambulant maintenance treatment of chronic schizophrenics [Studio in doppio cieco della flufenazina decanoato versus placebo nella terapia ambulatoriale di mantenimento di pazienti schizofrenici cronici]. *Rivista di Psichiatria* 1979;14: 374-83.
18. Eberhard G, Hellbom E. Haloperidol decanoate and flupenthixol decanoate in schizophrenia. A long-term double-blind cross-over comparison. *Acta psychiatrica Scandinavica* 1986; **74**(3): 255-62.
19. Guy Edwards J, Alexander JR, Alexander MS, Gordon A, Zutchi T. Controlled trial of sulpiride in chronic schizophrenic patients. *British Journal of Psychiatry* 1980;137:522-9.
20. Eklund K, Forsman A. Minimal effective dose and relapse--double-blind trial: haloperidol decanoate vs. placebo. *Clinical neuropharmacology* 1991; **14** Suppl 2: S7-12; discussion S-5.
21. Gaebel W, Schreiner A, Bergmans P, et al. Relapse prevention in schizophrenia and schizoaffective disorder with risperidone long-acting injectable vs quetiapine: results of a long-term, open-label,

- randomized clinical trial. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 2010; **35**(12): 2367-77.
22. Glick ID, Marder SR. Long-term maintenance therapy with quetiapine versus haloperidol decanoate in patients with schizophrenia or schizoaffective disorder. *The Journal of clinical psychiatry* 2005; **66**(5): 638-41.
  23. Hamilton SH, Edgell ET, Revicki DA, Breier A. Functional outcomes in schizophrenia: a comparison of olanzapine and haloperidol in a European sample. *International clinical psychopharmacology* 2000; **15**(5): 245-55.
  24. Hirsch SR, Gajendran R, Rohde PD, Stevens BC, Wing JK. Outpatient maintenance of chronic schizophrenic patients with long-acting fluphenazine: double-blind placebo trial. Report to the Medical Research Council Committee on Clinical Trials in Psychiatry. *British medical journal* 1973; **1**(5854): 633-7.
  25. Hogarty GE, Goldberg SC. Drug and sociotherapy in the aftercare of schizophrenic patients. One-year relapse rates. *Archives of general psychiatry* 1973; **28**(1): 54-64.
  26. Hollister LE, Erickson GV, Motzenbecker FP. Trifluoperazine in chronic psychiatric patients. *Journal of clinical and experimental psychopathology & quarterly review of psychiatry and neurology* 1960; **21**: 15-24.
  27. Hough D, Gopal S, Vijapurkar U, Lim P, Morozova M, Eerdeken M (2010). Paliperidone palmitate maintenance treatment in delaying the time-to-relapse in patients with schizophrenia: a randomized, double-blind, placebocontrolled study. *Schizophr Res* 116:107–117.
  28. Kahn RS, Fleischhacker WW, Boter H, et al. Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. *Lancet* 2008; **371**(9618): 1085-97.
  29. Keefe RS, Young CA, Rock SL, et al. One-year double-blind study of the neurocognitive efficacy of olanzapine, risperidone, and haloperidol in schizophrenia. *Schizophrenia research* 2006; **81**(1): 1-15.
  30. Kelly HB, Freeman HL, Banning B, Schiff AA. Clinical and social comparison of fluphenazine decanoate and flupenthixol decanoate in the community maintenance therapy of schizophrenia. *International pharmacopsychiatry* 1977; **12**(1): 54-64.
  31. Keskiner A, Holden JM, Itil TM. Maintenance treatment of schizophrenic outpatients with a depot phenothiazine. *Psychosomatics* 1968; **9**(3): 166-71.
  32. Kramer M, Simpson G, Maciulis V, et al. Paliperidone extended-release tablets for prevention of symptom recurrence in patients with schizophrenia: a randomized, double-blind, placebo-controlled study. *Journal of clinical psychopharmacology* 2007; **27**(1): 6-14.
  33. Leong OK, Wong KE, Tay WK, Gill RC. A comparative study of pipothiazine palmitate and fluphenazine decanoate in the maintenance of remission of schizophrenia. *Singapore medical journal* 1989; **30**(5): 436-40.
  34. Macfadden W, Ma YW, Thomas Haskins J, Bossie CA, Alphs L. A Prospective Study Comparing the Long-term Effectiveness of Injectable Risperidone Long-acting Therapy and Oral Aripiprazole in Patients with Schizophrenia. *Psychiatry* 2010; **7**(11): 23-31.
  35. Marder SR, Glynn SM, Wirshing WC, et al. Maintenance treatment of schizophrenia with risperidone or haloperidol: 2-year outcomes. *The American journal of psychiatry* 2003; **160**(8): 1405-12.
  36. McEvoy JP, Byerly M, Hamer RM, et al. Effectiveness of paliperidone palmitate vs haloperidol decanoate for maintenance treatment of schizophrenia: a randomized clinical trial. *Jama* 2014; **311**(19): 1978-87.
  37. Nishikawa T, Tsuda A, Tanaka M, Koga I, Uchida Y. Prophylactic effect of neuroleptics in symptom-free schizophrenics. *Psychopharmacology* 1982; **77**(4): 301-4.
  38. Nishikawa T, Tsuda A, Tanaka M, Hoaki Y, Koga I, Uchida Y. Prophylactic effect of neuroleptics in symptom-free schizophrenics: a comparative dose-response study of haloperidol and propericiazine. *Psychopharmacology* 1984; **82**(3): 153-6.
  39. Odejide OA, Aderounmu AF. Double-blind placebo substitution: withdrawal of fluphenazine decanoate in schizophrenic patients. *The Journal of clinical psychiatry* 1982; **43**(5): 195-6.
  40. Ota KY, Kurland AA. A double-blind comparison of haloperidol oral concentrate, haloperidol solutabs and placebo in the treatment of chronic schizophrenia. *The Journal of clinical pharmacology and new drugs* 1973; **13**(2): 99-110.
  41. Peuskens J, Trivedi J, Malyarov S, et al. Prevention of schizophrenia relapse with extended release quetiapine fumarate dosed once daily: a randomized, placebo-controlled trial in clinically stable patients. *Psychiatry* 2007; **4**(11): 34-50.
  42. Pigott TA, Carson WH, Saha AR, et al. Aripiprazole for the prevention of relapse in stabilized patients with chronic schizophrenia: a placebo-controlled 26-week study. *The Journal of clinical psychiatry* 2003; **64**(9): 1048-56.

43. Prien RF, Cole JO, Belkin NF. Relapse in chronic schizophrenics following abrupt withdrawal of tranquillizing medication. *The British journal of psychiatry : the journal of mental science* 1969; **115**(523): 679-86.
44. Rifkin A, Quitkin F, Klein DF. Fluphenazine decanoate, oral fluphenazine, and placebo in treatment of remitted schizophrenics. II. Rating scale data. *Archives of general psychiatry* 1977; **34**(10): 1215-9.
45. Rui Q, Wang Y, Liang S, et al. Relapse prevention study of paliperidone extended-release tablets in Chinese patients with schizophrenia. *Progress in neuro-psychopharmacology & biological psychiatry* 2014; **53**: 45-53.
46. Ruskin PE, Nyman G. Discontinuation of neuroleptic medication in older, outpatient schizophrenics. A placebo-controlled, double-blind trial. *The Journal of nervous and mental disease* 1991; **179**(4): 212-4.
47. Sampath G, Shah A, Krska J, Soni SD. Neuroleptic discontinuation in the very stable schizophrenic patient relapse rates and serum neuroleptic levels. *Human Psychopharmacology* 1992; **7**: 255-64.
48. Schiele BC, Vestre ND, Stein KE. A comparison of thioridazine, trifluoperazine, chlorpromazine, and placebo: a double-blind controlled study on the treatment of chronic, hospitalized, schizophrenic patients. *Journal of clinical and experimental psychopathology & quarterly review of psychiatry and neurology* 1961; **22**: 151-62.
49. Schooler N, Rabinowitz J, Davidson M, et al. Risperidone and haloperidol in first-episode psychosis: a long-term randomized trial. *The American journal of psychiatry* 2005; **162**(5): 947-53.
50. Serafetinides EA, Collins S, Clark ML. Haloperidol, clopenthixol, and chlorpromazine in chronic schizophrenia. Chemically unrelated antipsychotics as therapeutic alternatives. *The Journal of nervous and mental disease* 1972; **154**(1): 31-42.
51. Simon P, Fermanian J, Ginestet D, Goujet MA, Peron-Magnan P. Standard and long-acting depot neuroleptics in chronic schizophrenics: an 18-month open multicentric study. *Archives of general psychiatry* 1978; **35**(7): 893-7.
52. Steinert J, Neder A, Erba E, Pugh CR, Robinson C, Priest RG. A comparative trial of depot pipothiazine. *The Journal of international medical research* 1986; **14**(2): 72-7.
53. Tran PV, Hamilton SH, Kuntz AJ, et al. Double-blind comparison of olanzapine versus risperidone in the treatment of schizophrenia and other psychotic disorders. *Journal of clinical psychopharmacology* 1997; **17**(5): 407-18.
54. Tran PV, Dellva MA, Tollefson GD, Wentley AL, Beasley CM, Jr. Oral olanzapine versus oral haloperidol in the maintenance treatment of schizophrenia and related psychoses. *The British journal of psychiatry : the journal of mental science* 1998; **172**: 499-505.
55. Wistedt B, Koskinen T, Thelander S, Nerdrum T, Pedersen V, Molbjerg C. Zuclopenthixol decanoate and haloperidol decanoate in chronic schizophrenia: a double-blind multicentre study. *Acta psychiatrica Scandinavica* 1991; **84**(1): 14-21.
56. Zissis NP, Psaras M, Lyketsos G. Haloperidol decanoate, a new long-acting antipsychotic, in chronic schizophrenics: double-blind comparison with placebo. *Current Therapeutic Research* 1982; **31**: 650-5.

**Table DS1 Summary of RCTs included in this systematic review and network meta-analysis**

Trial	Reference	Country	Design	Wks	Subjects (N)	Age (yrs)	Setting	Treatments	Relapse Definitions	Efficacy (%)		Dropout (%)	Safety (%)		Funding
										Relapse	Hospital		EPS	Wt-Gain	
1	Arato 2002	USA	RCT (DB)	52	278	49.7	Hospital	ZPS v PBO	i) CGI-I $\geq 6$ , or PANSS (7 of 8) $\geq 6$ on 2 days; ii) need for more treatment	38, 77	NR	57, 86	4, 6	NR	Corporate
2	Bai 2007	Taiwan	RCT (SB)	48	50	46.4	Hospital	RSP, RSP-LAI	NR	0, 8	NR	NR	NR	NR	Corporate
3	Beasley 2003	USA, Europe	RCT (DB)	52	326	35.7	OPD	OLZ v PBO	i) BPRS-P item inc. to $>4$ ; ii) hospitalization	6, 55	1, 11	13, 54	2, 4	6, 1	Corporate
4	Bechelli 1985	NR	RCT (DB)	26	41	32.0	OPD	PIP-LAI, HAL-LAI	BPRS worsening	10, 10	NR	10, 10	30, 33	NR	NR
5	Breier 2005	Europe, No Amer	RCT (DB)	28	548	39.0	OPD	OLZ, ZPS	PANSS inc. $\geq 20\%$ or CGI $\geq 1$ point	15, 25	NR	40, 58	0, 2	13, 2	Corporate
6	Cassano 1975	Italy	RCT (DB)	4	76	38.0	Hospital	SUL, HAL	Clinical Deterioration	9, 14	NR	21, 17	NR	NR	NR
7	Chen 2010	China	RCT (DB)	52	178	24.2	OPD	QTP v PBO	i) PANSS worsening; ii) CGI-S $\geq 3$ ; iii) CGI-I $\geq 5$	41, 79	6, 16	31, 20	19, 16	39, 34	Corporate
8	Colonna 2000	France	Open-RCT	52	488	37.5	OPD	AMS, HAL	Treatment changed or sustained BPRS $\leq 20\%$	59, 55	NR	45, 53	13, 28	11, 3	None
9	Crawford 1974	France	RCT (DB)	40	31	47.0	OPD	TFP, FLZ-LAI	Hospitalization	27, 0	27, 0	40, 14	NR	NR	None
10	Crespo-Facorro 2010	Spain	Open-RCT	52	166	27.4	Hosp+OPD	OLZ, RSP, HAL	i) Any BPRS item $>5$ ; ii) CGI-S $>6$ , CGI-G $>6$ ; iii) hospitalization; iv) suicide	19, 14, 11	NR	33, 35, 57	NR	NR	None
11	Csernansky 2002	USA	RCT (DB)	52	365	40.0	Hosp+OPD	RSP, HAL	i) Hospitalization; ii) increased care + PANSS-T inc. $\geq 25\%$ or by $\geq 10$ points if $\leq 40$ at intake; iii) self-injury; iv) suicidal/homicidal ideation; v) violence; vi) CGI-C of 6 or 7	34, 60	NR	NR	9, 18	NR	Corporate
12	de Sena 2003	Brazil	RCT	52	33	27.0	OPD	RSP, HAL	Hospitalization	30, 23	30, 23	NR	NR	NR	None
13	Deberdt 2008	USA	RCT (DB)	24	133	44.0	OPD	QTP, ONZ	i) Hospitalization; ii) $\geq 20\%$ worsening on PANSS-T + increased care; iii) $\geq 20\%$ worsening of PANSS-T + worsening of CGI-S by $\geq 1$ + CGI-S $\geq 4$	15, 12	8, 1	60, 30	NR	33, 54	Corporate
14	Dellva 1997	No Amer	RCT (DB)	46	58	36.0	OPD	OLZ v PBO	Hospitalization	29, 70	NR	40, 31	NR	NR	Corporate
15	Dencker 1973	Sweden	RCT (DB)	52	67	41.0	Hosp+OPD	PIP-LAI, FPZ-LAI	Global-rating deterioration	10, 18	NR	NR	NR	NR	None
16	Dencker 1980	Sweden	RCT (DB)	52	60	40.0	OPD	ZUC-LAI, FPZ-LAI	Clinically unimproved	10, 13	NR	10, 23	53, 67	NR	None
17	Dotti 1979	NR	RCT (DB)	36	20	NR	OPD	FPZ-LAI v PBO	Need more treatment	10, 30	NR	10, 30	NR	NR	NR
18	Eberhard 1986	Sweden	RCT (DB)	48	32	38.0	Hosp+OPD	FPZ-LAI, HAL-LAI	Symptomatic worsening	19, 19	NR	19, 19	NR	NR	None
19	Edwards 1980	UK	RCT (DB)	6	38	NR	Hospital	SUL v TRI	Symptomatic worsening	5, 5	NR	11, 5	NR	NR	NR
20	Eklund 1991	NR	RCT (DB)	48	43	51.7	Hosp+OPD	HAL-LAI v PBO	Clinical worsening	10, 70	NR	25, 70	NR	NR	NR

21	Gaebel 2010	Europe	Open-RCT	104	710	41.6	D NR	RSP-LAI, QTP	i) Hospitalization; ii) more care + PANSS inc. $\geq 25\%$ or 10 pts if baseline $\leq 40$ ; iii) self-injury; iv) suicidal/homicidal ideation; v) violence; vi) CGI-C $\geq 6$ ; vii) exceeding protocol dose	17, 31	10, 17	54, 64	10, 6	10, 6	Corporate
22	Glick 2005	USA	RCT (DB)	48	29	42.7	OPD	HAL-LAI, QTP	Symptomatic worsening	60, 55	NR	50, 63	NR	NR	Corporate
23	Hamilton 2000	Europe	RCT (DB)	46	423	38.0	Hosp+OP D	OLZ, HAL	Hospitalization	20, 40	20, 40	48, 64	NR	NR	Corporate
24	Hirsch 1973	UK	RCT (DB)	28	81	43.5	OPD	FPZ-LAI v PBO	Clinical deterioration + change of treatment	8, 66	19, 58	18, 68	NR	NR	None
25	Hogarty 1973	USA	RCT (DB)	52	374	34.0	OPD	CPZ v PBO	Clinical deterioration	33, 73	8, 18	NR	NR	NR	US NIMH
26	Hollister 1960	NR	RCT (DB)	16	40	36.0	NR	TFP, CPZ	NR	20, 10	NR	NR	NR	NR	NR
27	Hough 2010	Europe, No Amer, Korea, Taiwan	RCT (DB)	NR	408	39.1	NR	PAL-LAI v PBO	i) Hospitalization; ii) PASS-T inc. $\geq 25\%$ x 2 days or $\geq 10$ -point inc. if initially $\leq 40$ ; iii) self-injury, or suicidal/homicidal ideation, aggression, iv) PANSS items to $\geq 5$ on 2 days or to $\geq 6$ if $\leq 4$ at intake	18, 48	NR	NR	6, 2	6, 3	Corporate
28	Kahn 2008	Europe and Israel	Open-RCT	52	351	26.0	NR	AMS, OLZ, QTP, ZPS, HAL	Hospitalized	16, 20, 23, 7, 22	16, 20, 23, 7, 22	31, 29, 49, 38, 61	37, 16, 25, 47, 64	63, 86, 65, 37, 53	Corporate
29	Keefe 2006	No Amer	RCT (DB)	52	414	39.0	Hosp+OP D	RSP, ONZ, HAL	i) PANSS score $\geq 4$ after inc. $\geq 2$ on any PANSS-P item; ii) PANSS-P items $\geq 4$ + inc. $\geq 4$ on PANSS-P subscale; iii) hospitalization	22, 12, 22	NR	66, 60, 72	20, 17, 38	11, 14, 2	Corporate
30	Kelly 1977	NR	RCT (DB)	36	60	42.0	OPD	FPX-LAI, FPZ-LAI	NR	12, 11	NR	NR	NR	NR	NR
31	Keskiner 1968	NR	RCT (DB)	12	24	36.0	OPD	FPZ-LAI v PBO	Clinical deterioration + more treatment	23, 73	8, 18	0, 0	4, 5	NR	NR
32	Kramer 2007	USA, Asia, Europe	RCT (DB)	52	207	38.3	OPD	PAL v PBO	i) hospitalization; ii) PANSS-T inc. $\geq 25\%$ 2 days or $\geq 10$ -points if $\leq 40$ at intake; iii) CGI-S inc. $\geq 4$ or to $\geq 5$ $\leq 4$ at intake randomisation, for 2 days; iv) self-injury, suicidal/homicidal ideation or aggression; v) PANSS items inc. to $\geq 5$ or to $\geq 6$ if 4 at intake randomization, for 2 days	22, 52	NR	41, 59	7, 3	18, 11	Corporate
33	Leong 1989	Singapore	RCT (DB)	28	60	37.8	OPD	PIP-LAI, FPZ-LAI	BPRS worsening	20, 20	NR	3, 0	0, 13	NR	None
34	Macfadden 2010	USA, Asia	RCT (DB)	104	349	37.8	OPD	RSP-LAI, APZ	i) hospitalization or inc. treatment; ii) PANSS-T inc. $\geq 25\%$ + $\geq 10$ points + CGI-S $\geq 4$ ;	46, 44	NR	30, 28	40, 35	NR	Corporate

									iii) self-injury, suicidal/homicidal ideation, violence; iv) change of ineffective treatment; v) drug dose above protocol limit						
35	Marder 2003	USA	RCT (DB)	104	63	43.0	OPD	RSP, HAL	Psychotic exacerbation, BPRS worsening >4	12, 27	NR	42. v 60	9, 27	NR	None
36	McEvoy 2014	USA	RCT (DB)	104	311	44.0	Hosp+OPD	PAL-LAI, HAL-LAI	i) hospitalization; ii) crisis intervention; iii) more OPD visits; iv) increased med. supplements	33, 32	30, 23	71, 69	14, 25	33, 22	US NIMH
37	Nishikawa 1982	Japan	RCT (DB)	156	30	33.2	OPD	CPZ, HAL v PBO	Insomnia, anxious, restless, excited, more psychotic	88, 82, 100	NR	NR	NR	NR	None
38	Nishikawa 1984	Japan	RCT (DB)	52	50	39.5	OPD	HAL v PBO	Insomnia, anxious, restless, excited, more psychotic	57, 100	NR	NR	NR	NR	None
39	Odejide 1982	NR	RCT (DB)	52	70	NR	OPD	FLZ-LAI v PBO	Hospitalization or major treatment change	14, 43	NR	40, 66	11, 3	NR	NR
40	Ota 1973	USA	RCT (DB)	12	44	42.5	Hospital	HAL v PBO	Clinical deterioration	39, 44	NR	3, 25	48, 31	NR	Corporate
41	Peuskens 2007	Europe, Asia	RCT (DB)	52	197	35.0	OPD	QTP v PBO	i) hospitalization; ii) PANSS inc. $\geq 30\%$ ; iii) CGI-I score $\geq 6$ ; iv) inc. treatment	12, 49	NR	17, 62	NR	5, 1	Corporate
42	Pigott 2003	USA, Europe	RCT (DB)	26	310	42.0	Hosp+OPD	APZ v PBO	i) CGI $\geq 5$ ; ii) PANSS hostility or uncooperativeness $\geq 5$ on 2 days; iii) PANSS-T inc. $\geq 20\%$	37, 61	7, 6	55, 72	3, 5	6, 4	Corporate
43	Prien 1968	USA	RCT (DB)	24	143	41.6	Hospital	CPZ v PBO	Global worsening	21, 42	NR	7, 18	12, 12	NR	US PHS
44	Rifkin 1977	USA	RCT (DB)	52	62	23.2	OPD	FPZ-LAI v PBO	Clinical deterioration + more social impairment	5, 68	NR	16, 16	26, 5	NR	US NIMH
45	Rui 2014	China	RCT (DB)	56	135	31.7	NR	PAL v PBO	i) hospitalization; ii) suicidal/homicidal ideation, self-injury, violence; iii) PANSS-T inc. $\geq 25\%$ or $\geq 10$ -points on 2 days if initial score $\leq 40$ iv) increase in individual PANSS items inc. to $\geq 5$ on 2 days or to $\geq 6$ if initial score $\leq 4$	30, 92	2, 6	0, 1	9, 4	42, 30	Corporate
46	Ruskin 1991	USA	RCT (DB)	24	23	60.1	OPD	HAL v PBO	Clinical worsening, insomnia, anxiety	9, 42	0, 8	27, 17	NR	NR	US VA
47	Sampath 1992	UK	RCT (DB)	52	24	57.4	Hospital	FLZ-LAI v PBO	BPRS-T inc. $\geq 25\%$ + Psychotic Inpatient Profile-based nursing judgment	33, 75	NR	NR	NR	NR	Public
48	Schiele 1961	Single-center	RCT (DB)	16	80	40.6	Hospital	TFP, CPZ v PBO	Global worsening	0, 0, 60	NR	5, 0, 5	35, 10, 5	NR	NR
49	Schooler 2005	Europe, No Amer, Australia, N	RCT (DB)	104	555	25.2	OPD	RSP, HAL	i) PANSS inc. $\geq 25\%$ or $\geq 10$ points if initial score $\leq 40$ ; ii) CGI-C "much or very much worse"; iii) suicidal/homicidal	42, 55	NR	42, 36	10, 18	76, 74	Corporate



		Zealand							ideation, self-injury, suicide; iv) violence						
50	Serafetinides 1972	USA	RCT (DB)	12	57	41.5	Hospital	CPZ, HAL v PBO	Symptom deterioration	43, 0, 23	NR	21, 0, 8	43, 43, 8	NR	NR
51	Simon 1978	France	Open RCT	72	181	NR	Hospital	PIP-LAI v FLZ-LAI	Symptom deterioration	13,7	NR	25, 25	5,1	NR	None
52	Steinert 1986	NR	RCT (DB)	52	39	42.5	NR	PIP-LAI, FPT-LAI	BPRS worsening	39, 44	NR	39, 44	NR	NR	NR
53	Tran 1997	Europe, USA, So Africa	RCT (DB)	28	339	36.0	Hosp+OPD	OLZ, RSP	i) PANSS-T inc. $\geq 20\%$ ; ii) CGI-S $\geq 3$	12, 32	NR	NR	19, 31	NR	Corporate
54	Tran 1998	No Amer	RCT (DB)	46	807	37.0	OPD	OLZ, HAL	Hospitalization	14, 9	NR	50, 58	NR	NR	Corporate
55	Wistedt 1991	Finland, Sweden	RCT (DB)	36	64	38.0	OPD	ZUC-LAI, HAL-LAI	Symptom deterioration	0, 14	NR	8, 18	25, 43	NR	None
56	Zissis 1982	NR	RCT (DB)	16	32	46.5	Hospital	HAL-LAI v PBO	Need to add HAL	31, 81	NR	0, 75	NR	NR	NR

Amisulpride: AML, aripiprazole: ARI, chlorpromazine: CHL, flupenthixol decanoate: FLX LAI, fluphenazine decanoate: FLZ LAI, haloperidol: HAL, haloperidol decanoate: HAL LAI, olanzapine: OLA, paliperidone: PAL, paliperidone depot: PAL LAI, placebo: PBO, pipothiazinepalmitate: PIP LAI, quetiapine: QUE, risperidone: RIS, risperidone depot: RIS LAI, sulphiride: SUL, trifluoperazine: TRI, ziprasidone: ZIP and zuclopenthixol decanoate: ZUC LAI

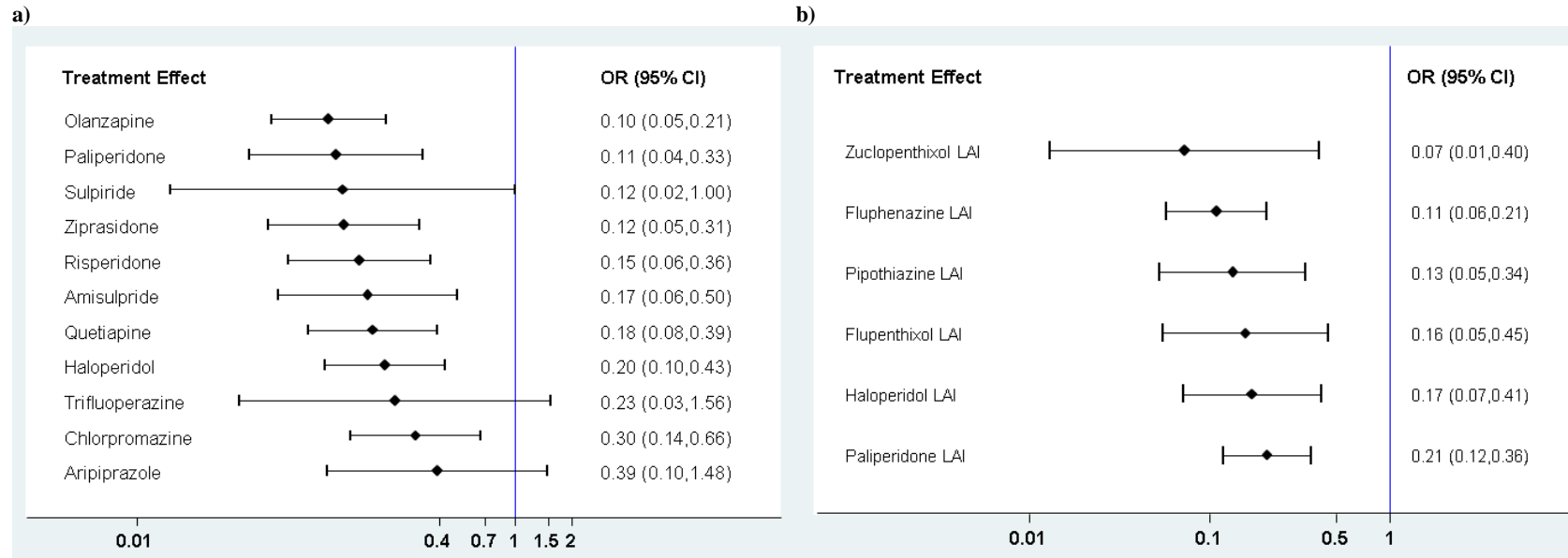
**Table DS2 Summary of excluded studies**

<b>No.</b>	<b>Excluded studies (Authors Year)</b>	<b>Reasons for exclusion</b>
1	Addington 2009	Outcome: no relapse rate reported
2	Blackburn 1981	Intervention: combination of prochlorpromazine, perphenazine, chlorpromazine, promazine and trifluoperazine
3	Boonstra 2011	Intervention: combination of olanzapine, risperidone and quetiapine
4	Buckley 2014	Intervention: combination of oral antipsychotic drugs
5	Casey 2003	Others: duplicate record with Pigott 2003
6	Chouinard 1978	Intervention: pipothiazinepalmitate, fluphenazine enanthate
7	Crespo-Facorro 2012	Outcome: no relapse rate reported
8	Crow 1986	Intervention: combination of flupenthixoli.m., chlorpromazine, haloperidol, pimozide and trifluoperazine
9	Dollfus 2005	Population: patients with post-psychotic depression
10	Elie 1975	Others: not written in English
11	Fleischhacker 2009	Outcome: no relapse rate reported
12	Freeman 1962	Others: not written in English
13	Fu 2015	Population: patients with schizoaffective disorder
14	Gopal 2011	Study design: open-label design
15	Gross 1960	Others: unable to retrieve article
16	Gross 1974	Intervention: combination of pimozide and trifluoperazine
17	Goldberg 1981	Others: unable to retrieve article
18	Huttunen 1996	Others: unable to retrieve article
19	Hui 2013	Study design: post hoc analysis of Chen 2010
20	Kane 2003	Outcome: no relapse rate reported
21	Kane 2009	Outcome: no relapse rate reported
22	Kasper 2003	Outcome: no relapse rate reported
23	Keks 2007	Outcome: no relapse rate reported
24	Kozma 2011	Study design: post hoc analysis of Hough 2010
25	Lecrubier 2006	Population: patients with negative symptoms
26	Lee 2010	Intervention: aripiprazole and non-aripiprazole antipsychotic drugs
27	Leff 1971	Intervention: combination of trifluoperazine and chlorpromazine
28	Levine 1980	Intervention: combination of oral and long-acting fluphenazine
29	Lieberman 2005	Outcome: no relapse rate reported
30	Loo 1997	Population: patients with negative symptoms
31	Lundin 1990	Outcome: no relapse rate reported
32	Marder 1987	Intervention: multi-dose study of fluphenazine decanoate
33	Marjerrison 1964	Intervention: combination of trifluoperazine or chlorprothixene
34	Morton 1968	Intervention: combination of chlorpromazine or trifluoperazine
35	Nasrallah 2010	Outcome: no relapse rate reported
36	Printo 1979	Outcome: no relapse rate reported
37	Rappaport 1978	Population: patients with acute schizophrenia
38	Rosenheck 2011	Intervention: oral and long-acting risperidone
39	rouillon 2008	Intervention: multi-dose study of olanzapine
40	Rouillon 2013	Others: unable to retrieve article
41	San 2012	Outcome: no relapse rate reported
42	Shrivastava 2000	Others: unable to retrieve article
43	Simpson 2006	Intervention: multi-dose study of risperidone
44	Speller 1997	Population: patients with negative symptoms
45	Spohn 1986	Intervention: combination of antipsychotic drugs
46	Smeraldi 2013	Study design: post-hoc analysis of Gaebel 2010
47	Stroup 2006	Outcome: no relapse rate reported
48	Velligan 2002	Outcome: no relapse rate reported
49	Wistedt 1981	Intervention: combination of fluphenazine or flupenthixol
50	Wistedt 1982	Others: duplicate record with Wistedt 1981

**Fig. DS1 Risk of bias assessment**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Arato 2002	●	?	?	?	●	●	●
Bai 2007	?	?	?	?	?	●	?
Beasley 2003	?	?	?	?	●	●	●
Bechelli 1985	?	?	?	?	?	?	?
Breier 2005	?	?	?	?	●	●	●
Cassano 1975	?	?	?	?	?	?	?
Chen 2010	●	●	●	●	●	●	?
Colonna 2000	?	?	?	?	●	?	?
Crawford 1974	?	?	●	●	●	?	?
Crespo-Facorro 2010	●	?	●	●	?	?	●
Csermanský 2002	?	?	?	?	●	●	?
Deberdt 2008	?	?	?	?	●	●	?
Delva 1997	?	?	?	?	●	?	●
Dencker 1973	?	?	●	●	?	?	●
Dencker 1980	?	?	●	●	●	?	?
De Sena 2003	●	?	?	?	?	?	●
Doddi 1979	?	?	●	●	?	●	●
Eberhard 1986	?	?	?	?	●	●	?
Edwards 1980	?	?	?	?	?	?	?
Eklund 1991	?	?	?	?	●	●	●
Gaebel 2010	?	?	●	●	●	●	?
Glick 2005	?	?	●	●	●	●	?
Hamilton 2000	?	?	?	?	●	?	●
Hirsch 1973	?	?	●	●	●	●	●
Hogarty 1973	?	?	●	?	●	●	?
Hollister 1960	?	?	●	?	?	●	●
Hough 2010	●	?	?	?	?	●	●
Kahn 2008	●	?	●	●	●	●	?
Keefe 2006	?	?	?	?	●	?	?
Kelly 1977	?	?	?	?	●	●	●
Keskner 1968	?	?	●	?	●	●	?
Kramer 2007	●	?	●	●	●	●	●
Leong 1989	?	?	●	●	?	?	?
Macfadden 2010	?	?	●	●	●	●	●
Marder 2003	?	?	?	?	●	●	●
McEvoy 2014	●	?	●	●	?	?	●
Nishikawa 1982	?	?	●	?	?	●	?
Nishikawa 1984	?	?	●	?	?	●	?
Odejide 1982	●	?	●	●	●	●	?
Ota 1973	?	?	?	?	?	●	●
Peuskens 2007	?	?	?	?	●	●	●
Pigott 2003	?	?	?	?	●	●	●
Prien 1968	?	?	?	?	●	●	?
Rifkin 1977	?	?	?	?	●	?	●
Rui 2014	?	?	?	?	●	?	●
Ruskin 1991	?	?	●	●	●	●	●
Sampath 1992	?	●	●	?	?	●	●
Schiele 1961	?	●	●	?	?	●	●
Schooler 2005	●	?	?	?	●	●	●
Serafetinides 1972	?	?	●	●	●	●	?
Simon 1978	?	?	●	●	?	?	?
Steinert 1986	?	?	●	●	●	●	?
Tran 1997	?	?	?	?	?	?	●
Tran 1998	?	?	?	?	●	?	?
Wistedt 1991	?	?	●	●	●	?	?
Zissis 1982	●	●	?	?	●	●	●

**Fig. DS2 Relapse rates of oral (a) and long-acting (b) antipsychotics compared with placebo**



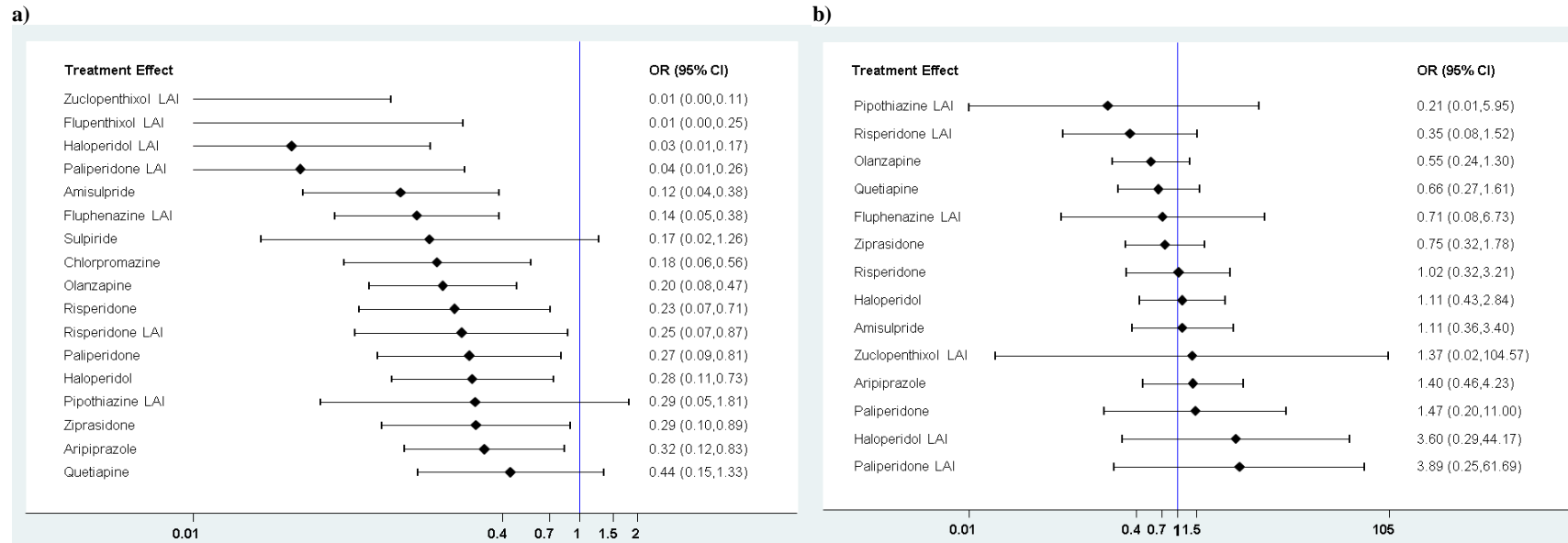
OR: odds ratio; 95% CI: 95% confidence interval

**Fig. DS3 Rehospitalization rates on antipsychotics**

<b>PBO</b>												
<b>0.13</b> (0.03,0.50)	<b>AMI</b>											
1.24 (0.38,4.03)	<b>9.60</b> (1.59,58.04)	<b>ARI</b>										
0.42 (0.16,1.09)	3.24 (0.61,17.12)	0.34 (0.07,1.55)	<b>CHL</b>									
<b>0.20</b> (0.06,0.65)	1.57 (0.26,9.41)	<b>0.16</b> (0.03,0.86)	0.48 (0.11,2.19)	<b>FLZ LAI</b>								
<b>0.23</b> (0.07,0.74)	1.77 (0.65,4.82)	<b>0.18</b> (0.03,0.98)	0.55 (0.12,2.50)	1.13 (0.21,5.95)	<b>HAL</b>							
<b>0.12</b> (0.04,0.35)	0.90 (0.34,2.41)	<b>0.09</b> (0.02,0.48)	0.28 (0.06,1.21)	0.57 (0.11,2.89)	<b>0.51</b> (0.26,0.99)	<b>OLA</b>						
0.27 (0.03,2.77)	2.06 (0.14,30.87)	0.21 (0.02,2.95)	0.64 (0.05,7.98)	1.31 (0.10,17.91)	1.16 (0.08,16.04)	2.28 (0.17,30.52)	<b>PAL</b>					
<b>0.28</b> (0.10,0.78)	2.13 (0.75,6.04)	0.22 (0.05,1.08)	0.66 (0.16,2.72)	1.36 (0.28,6.46)	1.21 (0.51,2.86)	<b>2.36</b> (1.03,5.40)	1.03 (0.08,13.46)	<b>QUE</b>				
<b>0.18</b> (0.05,0.67)	1.40 (0.39,5.01)	<b>0.15</b> (0.02,0.85)	0.43 (0.08,2.18)	0.89 (0.16,5.05)	0.79 (0.26,2.37)	1.55 (0.51,4.67)	0.68 (0.05,9.90)	0.66 (0.29,1.49)	<b>RIS LAI</b>			
1.99 (0.07,56.39)	15.44 (0.42,570.06)	1.61 (0.05,55.71)	4.76 (0.15,154.24)	9.83 (0.43,225.83)	8.73 (0.25,303.58)	17.11 (0.50,581.34)	7.50 (0.13,444.01)	7.25 (0.22,240.29)	11.06 (0.31,398.19)	<b>TRI</b>		
<b>0.05</b> (0.01,0.24)	0.38 (0.09,1.51)	<b>0.04</b> (0.01,0.29)	<b>0.12</b> (0.02,0.75)	0.24 (0.03,1.73)	<b>0.21</b> (0.06,0.79)	0.42 (0.12,1.52)	0.18 (0.01,3.12)	<b>0.18</b> (0.05,0.68)	0.27 (0.06,1.25)	<b>0.02</b> (0.00,0.99)	<b>ZIP</b>	

Comparisons between treatments should be read from left to right and the odds ratio (OR) with 95% confidence interval (95% CI) in the cell is the comparison between the column-defining treatment and the row-defining treatment. OR less than 1 favours the row-defining treatment (lower triangle) and column-defining treatment (upper triangle). Significant results are in bold. Amisulpride: AMI, aripiprazole: ARI, chlorpromazine: CHL, fluphenazine decanoate: FLZ LAI, haloperidol: HAL, olanzapine: OLA, paliperidone: PAL, placebo: PBO, quetiapine: QUE, risperidone depot: RIS LAI, trifluoperazine: TRI and ziprasidone: ZIP

**Fig. DS4 Withdrawal due to inefficacy (a) and adverse events (b) of antipsychotics compared with placebo**



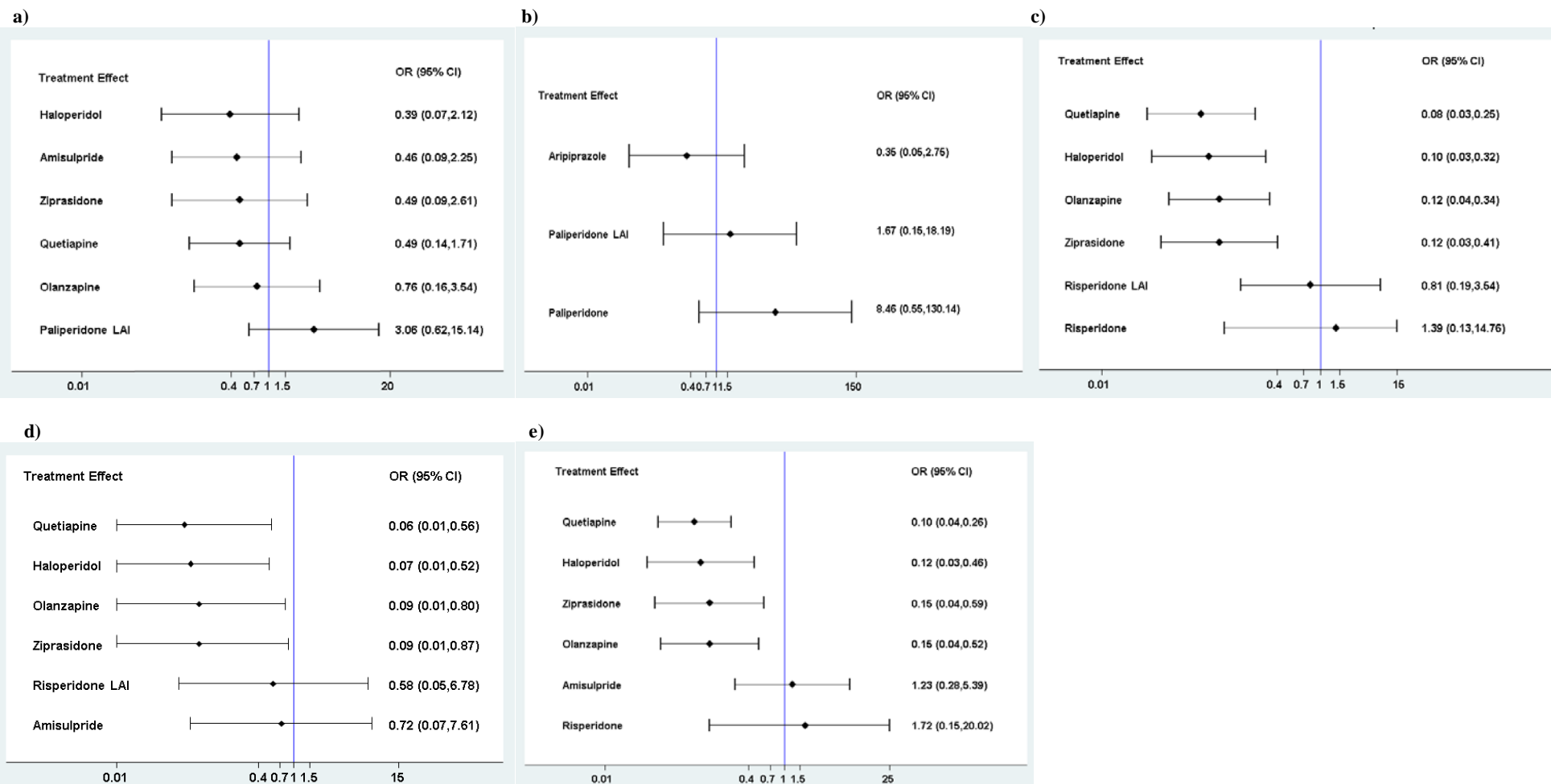
OR: odds ratio; 95% CI: 95% confidence interval

**Fig. DS5 Weight gain of antipsychotics**

PBO											
1.85 (0.57,5.99)	AMI										
1.53 (0.43,5.45)	0.83 (0.15,4.68)	ARI									
1.03 (0.34,3.14)	0.56 (0.25,1.22)	0.67 (0.12,3.64)	HAL								
1.18 (0.26,5.31)	0.64 (0.10,4.31)	0.77 (0.11,5.52)	1.15 (0.18,7.45)	HAL LAI							
<b>4.27</b> (1.53,11.95)	<b>2.31</b> (1.04,5.17)	2.79 (0.54,14.29)	<b>4.15</b> (1.97,8.71)	3.61 (0.59,22.23)	OLA						
1.75 (0.85,3.64)	0.95 (0.24,3.78)	1.14 (0.26,4.95)	1.70 (0.45,6.45)	1.48 (0.28,7.84)	0.41 (0.12,1.45)	PAL					
2.06 (0.61,6.97)	1.12 (0.21,6.07)	1.35 (0.23,7.82)	2.00 (0.38,10.43)	1.74 (0.72,4.19)	0.48 (0.10,2.38)	1.18 (0.29,4.87)	PAL LAI				
1.71 (0.74,3.94)	0.92 (0.39,2.20)	1.11 (0.24,5.09)	1.66 (0.71,3.84)	1.44 (0.26,8.02)	<b>0.40</b> (0.20,0.78)	0.97 (0.32,2.95)	0.83 (0.19,3.62)	QUE			
1.87 (0.54,6.44)	1.01 (0.40,2.58)	1.22 (0.21,7.18)	1.81 (0.88,3.74)	1.58 (0.23,10.49)	<b>0.44</b> (0.20,0.94)	1.07 (0.25,4.48)	0.90 (0.16,5.13)	1.09 (0.43,2.78)	RIS		
1.93 (0.55,6.76)	1.04 (0.29,3.74)	1.26 (0.21,7.50)	1.87 (0.53,6.58)	1.63 (0.23,11.51)	0.45 (0.14,1.42)	1.10 (0.26,4.69)	0.93 (0.16,5.36)	1.13 (0.44,2.88)	1.03 (0.28,3.87)	RIS LAI	
0.54 (0.17,1.77)	<b>0.29</b> (0.12,0.74)	0.36 (0.06,2.01)	0.53 (0.22,1.30)	0.45 (0.08,2.59)	<b>0.13</b> (0.06,0.27)	0.31 (0.08,1.24)	0.26 (0.05,1.44)	<b>0.32</b> (0.13,0.77)	<b>0.29</b> (0.11,0.79)	0.28 (0.08,1.02)	ZIP

Comparisons between treatments should be read from left to right and the odds ratio (OR) with 95% confidence interval (95% CI) in the cell is the comparison between the column-defining treatment and the row-defining treatment. OR less than 1 favours the row-defining treatment (lower triangle) and column-defining treatment (upper triangle). Significant results are in bold. Amisulpride: AMI, aripiprazole: ARI, chlorpromazine: CHL, haloperidol: HAL, haloperidol decanoate: HAL LAI, olanzapine: OLA, paliperidone: PAL, paliperidone depot: PAL LAI, placebo: PBO, quetiapine: QUE, risperidone: RIS, risperidone depot: RIS LAI and ziprasidone: ZIP

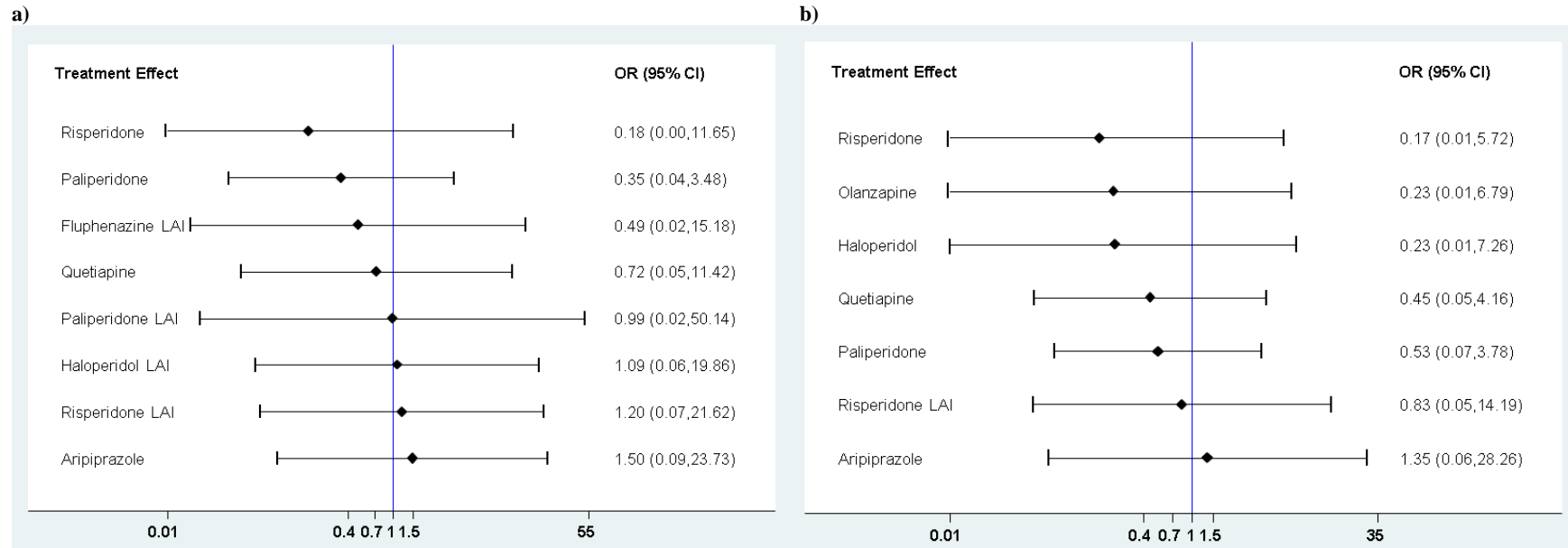
**Fig. DS6 Glucose intolerance (a) of antipsychotics compared to placebo and hyperprolactinemia (b–e) of antipsychotics compared to placebo, amisulpride, risperidone and risperidone-LAI**



OR: odds ratio; 95% CI: 95% confidence interval



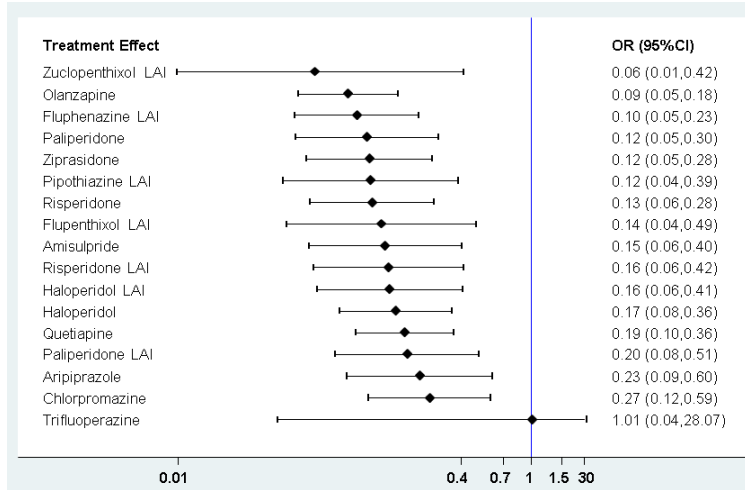
**Fig. DS7 Death (a) and suicide attempt (b) of antipsychotics relative to placebo**



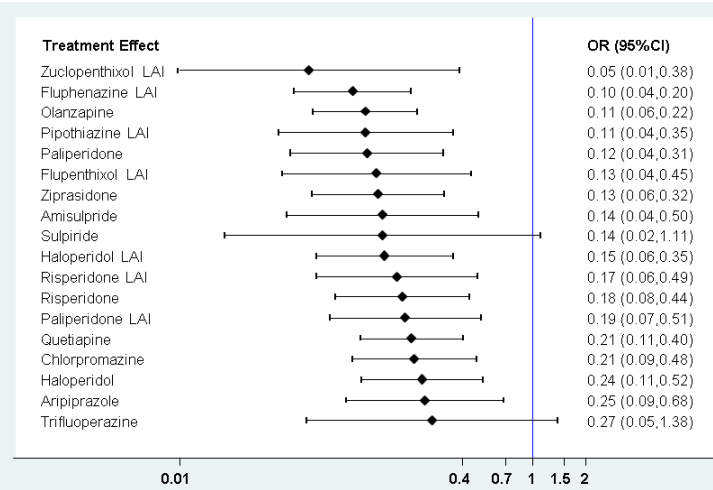
OR: odds ratio; 95% CI: 95% confidence interval

**Fig. DS8 Relapse rate of antipsychotics as compared to placebo by excluding trials with shorter duration trials (a), high dose of haloperidol (b) and published before 1980 (c)**

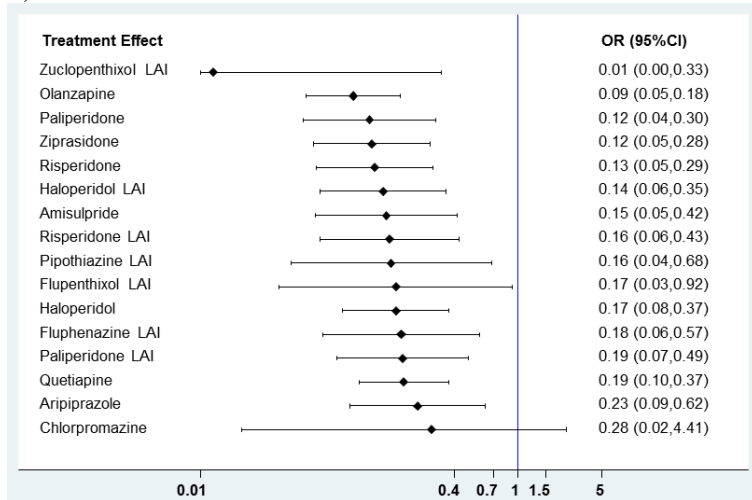
**a)**



**b)**

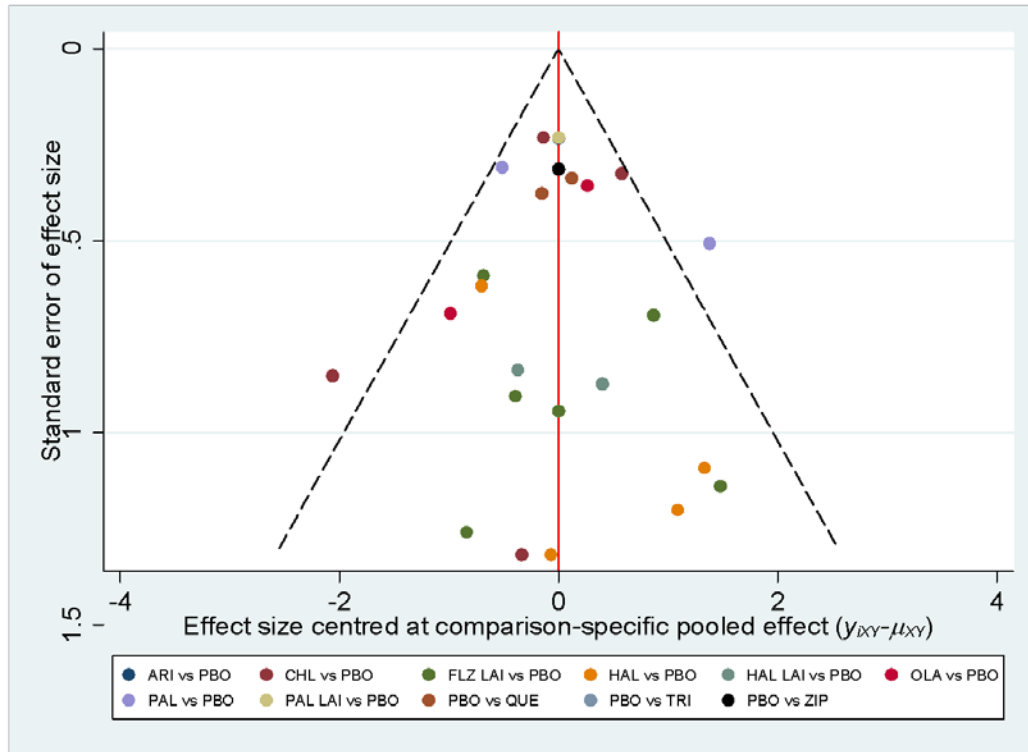


**c)**



OR: odds ratio; 95% CI: 95% confidence interval

Fig. DS9 Comparison-adjusted funnel plot



The red line represents the null hypothesis that the study-specific effect sizes do not differ from the respective comparison-specific pooled effect estimates for comparisons between antipsychotic treatments and placebo. Aripiprazole: ARI, chlorpromazine: CHL, fluphenazine decanoate: FLZ LAI, haloperidol: HAL, haloperidol decanoate: HAL LAI, olanzapine: OLA, paliperidone: PAL, paliperidone depot: PAL LAI, placebo: PBO, quetiapine: QUE, trifluoperazine: TRI and ziprasidone: ZIP