

G.10.1.3 Antipsychotics

Atypical antipsychotics vs placebo

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
NPI – lower numbers favours antipsychotics							

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
14 (Ma systematic review)*	Not serious	Not serious	Not serious	Not serious	2,970	MD -2.91 (-4.55, -1.28)	High
Brief psychiatric rating scale – lower numbers favours antipsychotics							
10 (Ma systematic review)*	Not serious	Not serious	Not serious	Not serious	1,957	MD -1.71 (-2.74, -0.68)	High
Cohen-Mansfield Agitation Inventory – lower numbers favours antipsychotics							
8 (Ma systematic review)*	Not serious	Serious ¹	Not serious	Not serious	2,161	MD -1.85 (-3.18, -0.51)	Moderate
Clinical Global Impression of Change – lower numbers favours antipsychotics							
11 (Ma systematic review)*	Not serious	Not serious	Not serious	Not serious	2,566	MD -0.30 (-0.43, -0.18)	High
Adverse events (extrapyramidal) – lower numbers favours antipsychotics							
15 (Ma systematic review)*	Not serious	Not serious	Not serious	Serious ²	4,092	RR 1.50 (1.24, 1.82)	Moderate
Adverse events (somnolence) – lower numbers favours antipsychotics							
12 (Ma systematic review)*	Not serious	Not serious	Not serious	Not serious	3,838	RR 2.48 (2.00, 3.07)	High
Adverse events (cerebrovascular) – lower numbers favours antipsychotics							
12 (Ma systematic review)*	Not serious	Not serious	Not serious	Serious ²	3,198	RR 2.24 (1.21, 4.16)	Moderate
Mortality – lower numbers favours antipsychotics							
17 (Ma systematic review)*	Not serious	Not serious	Not serious	Not serious	5,028	RR 1.53 (1.06, 2.22)	High
*Results from the Ma systematic review were converted from odds ratios to relative risks for consistency with the rest of the guideline, and corrections were made where analyses had not correctly accounted for trials with more than 2 arms.							
1. $i^2 > 40\%$.							
2. 95% CI crosses one line of a defined MID interval							

Olanzapine vs haloperidol

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
MMSE – higher numbers favour olanzapine							
1 (Verhey 2006)	Serious ¹	N/A	Not serious	Serious ²	46	MD 0.66 (-3.79, 5.11)	Low
NPI – lower numbers favour olanzapine							
1 (Verhey 2006)	Serious ¹	N/A	Not serious	Serious ²	45	MD 7.78 (-5.87, 21.43)	Low
CMAI – lower numbers favour olanzapine							
1 (Verhey 2006)	Serious ¹	N/A	Not serious	Serious ²	58	MD 6.50 (-2.45, 15.45)	Low
1. Aspects of study design poorly reported. 2. Non-significant result.							

Risperidone vs rivastigmine

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
CMAI – lower numbers favour risperidone							
1 (Holmes 2007)	Serious ¹	N/A	Not serious	Not serious	27	MD -22.90 (-36.85, -8.95)	Moderate
1. Aspects of study design poorly reported.							

Antipsychotic withdrawal

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
BPSD – lower numbers favour discontinuation							
3 (Pan systematic review)	Not serious	Serious ¹	Not serious	Serious ²	214	MD 0.19 (-0.20, 0.58)	Low
BPSD worsening – lower numbers favour discontinuation							
7 (Pan systematic review)	Not serious	Not serious	Not serious	Not serious	366	RR 1.78 (1.30, 2.42)	High
Early study termination – lower numbers favour discontinuation							
6 (Pan systematic review)	Not serious	Not serious	Not serious	Serious ³	462	RR 1.13 (0.88, 1.46)	Moderate
Mortality – lower numbers favour discontinuation							

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
5 (Pan systematic review)	Not serious	Not serious	Not serious	Serious ²	407	RR 0.79 (0.41, 1.54)	Moderate
<ol style="list-style-type: none"> 1. i^2 value > 40%. 2. Non-significant result. 3. 95% CI crosses one line of a defined MID interval. 							

Antipsychotic withdrawal UK (6 months)

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Cognition (SIB) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	102	MD -0.4 (-6.4, 5.5)	Moderate
Neuropsychiatric symptoms (NPI) – lower numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	109	MD -2.4 (-8.2, 3.5)	Moderate
Cognition (MMSE) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	84	MD -1.0 (-2.7, 0.7)	Moderate
Parkinsonism (modified UPDRS) – lower numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	84	MD 1.1 (-0.4, 2.6)	Moderate
Activities of daily living (Bristol ADL) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	106	MD 1.7 (-1.2, 4.6)	Moderate
Receptive language (STALD) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	73	MD -0.2 (-1.1, 0.6)	Moderate
Expressive skill (STALD) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	73	MD -1.0 (-2.0, 0.04)	Moderate
Verbal fluency (FAS) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Not serious	56	MD -4.5 (-7.3, -1.7)	High
<ol style="list-style-type: none"> 1. Non-significant result. 							

Antipsychotic withdrawal UK (12 months)

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Cognition (SIB) – higher numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Serious ¹	55	MD -8.4 (-18.6, 1.7)	Moderate
Neuropsychiatric symptoms (NPI) – lower numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Not serious	59	MD -10.9 (-20.1, -1.7)	High
1. Non-significant result.							

Antipsychotic withdrawal UK (24-54 months)

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Mortality (ITT) – lower numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Not serious	165	HR 0.58 (0.36, 0.92)	High
Mortality (modified ITT*) – lower numbers favour continuation							
1 (Ballard 2008)	Not serious	N/A	Not serious	Not serious	128	HR 0.58 (0.35, 0.95)	High
*Population restricted to only those individuals who took one dose of study medication							

Antipsychotic switch to memantine

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Bristol Activities of Daily Living score – higher numbers favour memantine							
1 (Ballard 2015)	Not serious	N/A	Not serious	Serious ¹	164	MD 0.23 (-1.80, 2.27)	Moderate
Cohen-Mansfield Agitation Inventory – lower numbers favour memantine							
1 (Ballard 2015)	Not serious	N/A	Not serious	Serious ¹	164	MD 4.09 (-0.35, 8.53)	Moderate
NPI – lower numbers favour memantine							
1 (Ballard 2015)	Not serious	N/A	Not serious	Serious ¹	163	MD 3.63 (-1.40, 8.67)	Moderate
MMSE – higher numbers favour memantine							
1 (Ballard 2015)	Not serious	N/A	Not serious	Serious ¹	113	MD 1.29 (-0.21, 2.79)	Moderate
Serious adverse events – lower numbers favour memantine							
1 (Ballard 2015)	Not serious	N/A	Not serious	Serious ²	164	RR 0.74 (0.44, 1.24)	Moderate

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Mortality – lower numbers favour memantine							
1 (Ballard 2015)	Not serious	N/A	Not serious	Serious ¹	164	RR 0.46 (0.15, 1.42)	Moderate
1. Non-significant result 2. 95% CI crosses one line of a defined MID interval 3. 95% CI crosses two lines of a defined MID interval							

Enhanced psychosocial care versus usual care

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Proportion taking neuroleptics – lower numbers favour intervention							
1 (Fossey)	Serious ¹	N/A	Not serious	Not serious	338	RR 0.55 (0.39, 0.76)	Moderate
Fall in past 12 months – lower numbers favour intervention							
1 (Fossey)	Serious ¹	N/A	Not serious	Very serious ³	340	RR 0.90 (0.59, 1.38)	Very low
Aggression (Cohen-Mansfield agitation score) – lower numbers favour intervention							
1 (Fossey)	Serious ¹	N/A	Not serious	Serious ²	334	MD 0.3 (-8.3, 8.9)	Low
Wellbeing (dementia care mapping) – higher numbers favour intervention							
1 (Fossey)	Serious ¹	N/A	Not serious	Serious ²	302	MD -0.2 (-0.5, 0.2)	Low
1. Lack of appropriate blinding 2. Non-significant result. 3. 95% CI crosses two lines of a defined MID interval							