Placebo controlled RCTs of atypical antipsychotics for the neuropsychiatric symptoms of dementia

Antipsychotic	**Participants**	**Primary results**	**Adverse events**
Olanzapine (1, 2.5, 5, or 7.5mg daily)	652 nursing home residents with AD	No significant difference in psychosis subscales of the NPI-NH or CGIC between olanzapine (any dose) and placebo.	Weight gain, urinary incontinence, and anorexia more common with olanzapine, but no difference in withdrawals (p=0.35), motor function, or anticholinergic effects
Olanzapine (5, 10, or 15mg daily)	206 nursing home residents with AD	Olanzapine 5 or 10mg improved sum of three core NPI-NH symptoms (delusion, hallucinations, agitation/aggression). No significant difference between 15mg olanzapine and placebo	More withdrawals (44% *v* 18%), somnolence 5–8 times greater, and gait disturbance 7.5–11 times more frequent with olanzapine
Olanzapine (2.5 or	204 people in	At 2 hours after injection,	No significant difference in adverse effects

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5.0mg im)	nursing homes or hospitals with AD, VaD, or mixed	olanzapine improved PANSS-EC compared with placebo	
Risperidone (0.5, 1.0, or 2.0mg daily)	625 nursing home residents with AD, VaD, or mixed	More people taking 1.0 or 2.0mg risperidone experienced at least a 50% improvement in BEHAVE-AD score (50% with 2mg *v* 45% with 1mg *v* 33% with placebo; p=0.002 for 2mg *v* placebo, p=0.02 for 1mg *v* placebo)	More withdrawals with 2mg risperidone than placebo (42% *v* 27%). Significant increase in extrapyramidal symptoms with 2mg risperidone. Increasing somnolence with increasing risperidone dose (8%–28%)
Risperidone (average dose 0.95mg daily)	345 nursing home residents with AD, VaD, or	Risperidone improved aggression compared with placebo (CMAI aggression subscale score (score	Serious adverse events more common with risperidone than placebo (16.8% *v* 8.8%). Serious adverse events included 5 strokes and 1 transient

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	mixed	range 14 to 98) difference: 4.4 points; p<0.001)	ischaemic attack in the risperidone group
Risperidone (average dose 1.1mg daily)	229 nursing home residents with AD, VD, or mixed	No significant difference between risperidone and placebo in proportion of people with at least a 30% improvement in BEHAVE-AD score	No significant difference in extrapyramidal symptoms, but increased somnolence with risperidone compared with placebo (12.2% *v* 4.4%)

AD, Alzheimer's disease; BEHAVE-AD, behavioural pathology in Alzheimer Disease Rating Scale; CGIC, Clinical Global Impression of Change; NPI-NH, Neuropsychiatric Inventory-Nursing Home version; im, intramuscular; PANSS-EC, positive and negative syndrome scale - excited component; VaD, vascular dementia.