Appendix K: Evidence Summary

Typical antipsychotics - treatment; hospital setting review; typical antipsychotics vs placebo / no treatment

Outcome	*Meta-analysis details*	*Summary Statistics*	*Comments:*	*GRADE details:*	*GRADE Comments*	*GRADE Evidence Rating*
Complete response	1trial; 101 patients; from RCT	RR=3.95 (95%CI 1.75, 8.9)	Statistically significant improvement of delirium in the haloperidol group on clinical global impression scale at 7 days	• Study quality: Good • Directness: Indirect outcome - delirium assessment method • Imprecision: Number of events < 300 • Inconsistency: consistent • Reporting bias: Adequate	It is unlikely pts blinded because of nature of the intervention (IM vs control); Clinical global impression scale- indirect method of assessment of delirium; Both groups received somatic treatment aiming at delirium. Large effect	Moderate
Duration of delirium	1trial; 101 patients; from RCT	MD=-1.78 (95%CI -2.86, -0.7)	Statistically significant shorter duration for the haloperidol group	• Study quality: Poor - some confounding • Directness: Direct • Imprecision: Wide CI • Inconsistency: consistent • Reporting bias: Adequate	Reported as 'time to take effect'. Duration of delirium was given for responders so potentially biased	very low
Severity of delirium	1trial; 101 patients; from RCT	MD=-10.4 (95%CI -13.95, -6.85)	Statistically significant: severity lower in the haloperidol group on the DRS (0-32)	• Study quality: Poor - not blinded • Directness: Direct • Imprecision: Number of patients < 400 • Inconsistency: consistent • Reporting bias: Adequate	DRS scale 0-32; MID (=20% = 6.4), i.e. CI precise, but fairly small number patients. Patients not blinded. Large effect	Moderate
Adverse event (extrapyramidal)	2 trials; 508 patients; from RCT	RR1	Neither study reported any extrapyramidal events	• Study quality: Good • Directness: Direct • Imprecision: Number of events < 300 • Inconsistency: consistent • Reporting bias: Adequate	Placebo comparison. Adverse events data from prevention trials. No extrapyramidal effects in either study. Smaller study not blinded.	Low
Adverse events (sedation)	1trial; 430 patients; from RCT	RR1	No sedation in either group	• Study quality: Good • Directness: Direct • Imprecision: Number of events < 300 • Inconsistency: consistent • Reporting bias: Adequate	Placebo comparison. Adverse events data from prevention trials. No sedation events reported.	Low

Atypical antipsychotics - treatment; hospital setting review; Atypical antipsychotics vs placebo / no treatment

Outcome	*Meta-analysis details*	*Summary Statistics*	*Comments:*	*GRADE details:*	*GRADE Comments*	*GRADE Evidence Rating*
Complete response	1trial; 103 patients; from RCT	RR=3.68 (95%CI 1.63, 8.33)	Significant difference in favour of the olanzapine group	● Study quality: Poor - not blinded ● Directness: Indirect outcome - delirium assessment method ● Imprecision: Number of events < 300 ● Inconsistency: consistent ● Reporting bias: Adequate	Measured on clinical global impression scale (GDG said this was indirect). All patients received "somatic treatment aiming at delirium". Patients not blinded; large effect	Moderate
Duration of delirium	1trial; 103 patients; from RCT	MD=-2.4 (95%CI -3.51, -1.29)	Statistically significant in favour of the olanzapine group	● Study quality: Poor - some confounding ● Directness: Direct ● Imprecision: Wide CI ● Inconsistency: consistent ● Reporting bias: Adequate	'Time to take effect' only given for responders only - i.e. likely to be confounded; All patients received somatic treatment aiming at delirium	very low
Severity of delirium	1trial; 103 patients; from RCT	MD=-11.1 (95%CI -14.51, -7.69)	Statistically significant difference on the DRS (0-32); some uncertainty	● Study quality: Poor - not blinded ● Directness: Direct ● Imprecision: Number of patients < 400 ● Inconsistency: consistent ● Reporting bias: Adequate	All patients received somatic treatment aiming at delirium; precise in terms of GRADE.. Patients not blinded; large effect	Moderate
Adverse events (sedation)	1trial; 79 patients; from Cohort	Proportion (%)30	High proportion of patients with sedation	● Study quality: ---- ● Directness: Indirect patients - minor, comorbidity ● Imprecision: ---- ● Inconsistency: ---- ● Reporting bias: ---	Olanzapine; Hospitalised cancer patients;clinical examination for adverse events	Low

Atypical antipsychotics - treatment; hospital setting review; atypical antipsychotic1 vs atypical antipsychotic2

Outcome	*Meta-analysis details*	*Summary Statistics*	*Comments:*	*GRADE details:*	*GRADE Comments*	*GRADE Evidence Rating*
Complete response	1trial; 31 patients; from RCT		No results for this outcome	• Study quality: Poor - incomplete follow up • Directness: Direct • Imprecision: Number of patients < 400 • Inconsistency: consistent • Reporting bias: Adequate	Very small study; 25% missing data in 1 arm. No results given	----
Duration of delirium	1trial; 31 patients; from RCT	MD=-1.1 (95%CI -4.09, 1.89)	No significant difference between amisulpride and quetiapine groups	• Study quality: Poor - incomplete follow up • Directness: Direct • Imprecision: Wide CI • Inconsistency: consistent • Reporting bias: Adequate	Lower Conf limit crosses 4x MID	very low
Severity of delirium	1trial; 31 patients; from RCT	MD=0 (95%CI -1.48, 1.48)	No significant difference on the DRS-R-98(0-39)between amisulpride and quetiapine groups	• Study quality: Poor - incomplete follow up • Directness: Direct • Imprecision: Number of patients < 400 • Inconsistency: consistent • Reporting bias: Adequate	Very small study; 25% missing data in 1 arm	Low

HT3 inhibitors- treatment; hospital setting review; typical antipsychotics vs placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*Comments:*	*GRADE details:*	*GRADE Comments*	*GRADE Evidence Rating*
Incidence of delirium-sensitivity analysis	1trial; 430 patients; from RCT	RR=0.91 (95%CI 0.59, 1.42)	No significant difference	• Study quality: Good • Directness: Direct • Imprecision: Precise • Inconsistency: consistent • Reporting bias: Adequate	Patients also received proactive geriatric consultation; Use of rescue meds may have led to confounding	High

Cross review - treatment; hospital setting review; typical antipsychotic vs atypical antipsychotic

Outcome	*Meta-analysis details*	*Summary Statistics*	*Comments:*	*GRADE details:*	*GRADE Comments*	*GRADE Evidence Rating*
Complete response	2 trials; 219 patients; from Meta analysis of RCTs	RR=0.99 (95%CI 0.8, 1.21); p=0.24; I2 =27%	No significant difference between haloperidol and olanzapine groups	• Study quality: Poor - not blinded • Directness: Indirect outcome - delirium assessment method • Imprecision: Number of events < 300 • Inconsistency: consistent • Reporting bias: Adequate	Haloperidol vs olanzapine. One study [32.4% weight] inadeq sequence generation & allocation concealment, funding, and outcome possibly inadequate. Patients unblinded in major study and indirect outcome measure	Low
Duration of delirium	1trial; 146 patients; from RCT	MD=0.62 (95%CI 0.06, 1.18)	Signifcantly shorter time to take effect for the olanzapine group compared to the haloperidol group	• Study quality: Very Poor • Directness: Direct • Imprecision: Number of patients < 400 • Inconsistency: consistent • Reporting bias: Adequate	Reported as 'time to take effect' in responders only - likely to be biased	very low
Severity of delirium	1trial; 146 patients; from RCT	MD=0.7 (95%CI -0.45, 1.85)	No significant difference between the haloperidol and the olanzapine groups on the DRS (0-32)	• Study quality: Poor - not blinded • Directness: Direct • Imprecision: Number of patients < 400 • Inconsistency: consistent • Reporting bias: Adequate	All patients received somatic treatment aiming at delirium; DRS scale 0-32, narrow CI, but fairly small trial. Patients not blinded.	Moderate
Adverse event (extrapyramidal)	1trial; 73 patients; from Quasi RCT	RR=8.2 (95%CI 0.48, 140.09)	No significant difference	• Study quality: Very Poor • Directness: Direct • Imprecision: Wide CI • Inconsistency: consistent • Reporting bias: Adequate	Haloperidol vs olanzapine; quasi randomised design; wide CI. Adverse events carefully recorded; not blinded	very low