Evidence Table D-25. Binary cardiac outcomes in studies comparing interventions to prevent development of delirium

| Author, year | Population | Intervention group, n | Control group, n | Route of administration | Outcome definition | n / N (%), intervention group | n / N (%), control group | Relative risk (95% CI) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First-generation antipsychotic vs. placebo |  |  |  |  |  |  |  |  |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Placebo (Planned dose: 2-8ml, loading dose 10ml over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Arrhythmia | 3 / 30 (10%) | 2 / 30 (7%) | 1.50 (0.27 to 8.34) |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Placebo (Planned dose: 2-8ml, loading dose 10ml over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Bradycardia (Heart rate decreased to ≤60 beats/min) | 2 / 30 (7%) | 1 / 30 (3%) | 2.00 (0.19 to 20.90) |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Placebo (Planned dose: 2-8ml, loading dose 10ml over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Hypotension | 3 / 30 (10%) | 3 / 30 (10%) | 1.00 (0.22 to 4.56) |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Placebo (Planned dose: 2-8ml, loading dose 10ml over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Prolongation in the QTc interval >500ms | 2 / 30 (7%) | 0 / 30 (0%) | 5.00 (0.25 to 99.95) |
| Al-Qadheeb, 2016[2](#_ENREF_2) | MV patients with subsyndromal delirium | Haloperidol (Planned dose: 1mg), 34 | Placebo (Planned dose: 5% dextroseml), 34 | Intravenous | Hypotension | 1 / 34 (2.9%) | 1 / 34 (2.9%) | 1.00 (0.07 to 15.34) |
| Al-Qadheeb, 2016[2](#_ENREF_2) | MV patients with subsyndromal delirium | Haloperidol (Planned dose: 1mg), 34 | Placebo (Planned dose: 5% dextroseml), 34 | Intravenous | Prolongation in the QTc interval | 4 / 34 (11.8%) | 1 / 34 (2.9%) | 4.00 (0.47 to 33.97) |
| Girard, 2010[4](#_ENREF_4) | > 18 years MV medical and surgical ICU patients | Haloperidol (Planned dose: 5 Median dose: 15 (10.8-17), 35 | Placebo (Planned dose: 5ml), 36 | Oral | Prolongation in the QTc interval prolongation of the QTc > 500 ms while receiving study drug | 2 / 35 (5.7%) | 3 / 36 (8.3%) | 0.69 (0.12 to 3.86) |
| Girard, 2010[4](#_ENREF_4) | > 18 years MV medical and surgical ICU patients | Haloperidol (Planned dose: 5 Median dose: 15 (10.8-17), 35 | Placebo (Planned dose: 5ml), 36 | Oral | Ventricular arrhythmias | 0 / 35 (%) | 0 / 36 (%) |   |

| Author, year | Population | Intervention group, n | Control group, n | Route of administration | Outcome definition | n / N (%), intervention group | n / N (%), control group | Relative risk (95% CI) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Khan, 2018[8](#_ENREF_8) | English speaking individuals undergoing thoracic surgery | Haloperidol (Planned dose: 0.5mg, Planned duration: 4 days (11 doses total)), 68 | Placebo (Planned dose: NR, Planned duration: 4 days (11 doses total)), 67 | Intravenous | Arrythmia | 9 / 68 (13.2%) | 10 / 67 (14.9%) | 0.89 (0.38 to 2.04) |
| Khan, 2018[8](#_ENREF_8) | English speaking individuals undergoing thoracic surgery | Haloperidol (Planned dose: 0.5mg, Planned duration: 4 days (11 doses total)), 68 | Placebo (Planned dose: NR, Planned duration: 4 days (11 doses total)), 67 | Intravenous | QT prolongation | 3 / 68 (4.4%) | 4 / 67 (6%) | 0.74 (0.17 to 3.18) |
| Khan, 2018[8](#_ENREF_8) | English speaking individuals undergoing thoracic surgery | Haloperidol (Planned dose: 0.5mg, Planned duration: 4 days (11 doses total)), 68 | Placebo (Planned dose: NR, Planned duration: 4 days (11 doses total)), 67 | Intravenous | Deep venous thrombosis | 1 / 68 (1.5%) | 5 / 67 (7.5%) | 0.2 (0.02 to 1.64) |
| Page, 2013[10](#_ENREF_10) | ICU patients needing MV within 72 hours of admission were enrolled | Haloperidol (Planned dose: 2.5mg), 71 | Placebo (Planned dose: 0.5ml), 70 | Intravenous | Atrial fibrillation | 7 / 71 (10%) | 3 / 70 (4%) | 2.30 (0.62 to 8.54) |
| Page, 2013[10](#_ENREF_10) | ICU patients needing MV within 72 hours of admission were enrolled | Haloperidol (Planned dose: 2.5mg), 71 | Placebo (Planned dose: 0.5ml), 70 | Intravenous | Bradycardia | 2 / 71 (3%) | 0 / 70 (%) | 4.93 (0.24 to 100.89) |
| Page, 2013[10](#_ENREF_10) | ICU patients needing MV within 72 hours of admission were enrolled | Haloperidol (Planned dose: 2.5mg), 71 | Placebo (Planned dose: 0.5ml), 70 | Intravenous | Hypotension | 3 / 71 (4%) | 2 / 70 (3%) | 1.48 (0.25 to 8.58) |
| Page, 2013[10](#_ENREF_10) | ICU patients needing MV within 72 hours of admission were enrolled | Haloperidol (Planned dose: 2.5mg), 71 | Placebo (Planned dose: 0.5ml), 70 | Intravenous | Prolongation in the QTc interval > 500 ms | 7 / 71 (10%) | 6 / 70 (9%) | 1.15 (0.41 to 3.25) |
| Page, 2013[10](#_ENREF_10) | ICU patients needing MV within 72 hours of admission were enrolled | Haloperidol (Planned dose: 2.5mg), 71 | Placebo (Planned dose: 0.5ml), 70 | Intravenous | Supraventricular Tachycardia | 4 / 71 (6%) | 1 / 70 (1%) | 3.94 (0.45 to 34.41) |

| Author, year | Population | Intervention group, n | Control group, n | Route of administration | Outcome definition | n / N (%), intervention group | n / N (%), control group | Relative risk (95% CI) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Schrijver, 2018[12](#_ENREF_12) | Medical and surgical patients | Haloperidol (Planned dose: 1mg), 118 | Placebo, 124 | Oral | Acute coronary syndrome | 2 / 118 (1.7%) | 2 / 124 (1.6%) | 1.05 (0.15 to 7.34) |
| Schrijver, 2018[12](#_ENREF_12) | Medical and surgical patients | Haloperidol (Planned dose: 1mg),  | Placebo,  | Oral | Prolongation in the QTc interval milliseconds | -8.5 (32.5%) | -5.5 (30%) | -2.92 (-12.42 to 6.59) |
| Schrijver, 2018[12](#_ENREF_12) | Medical and surgical patients | Haloperidol (Planned dose: 1mg),  | Placebo,  | Oral | Prolongation in the QTc interval milliseconds | 7.3 (35%) | -5.1 (45.5%) | 12.45 (-12.26 to 37.17) |
| Schrijver, 2018[12](#_ENREF_12) | Medical and surgical patients | Haloperidol (Planned dose: 1mg),  | Placebo,  | Oral | Prolongation in the QTc interval milliseconds | -6.4 (29.2) | 7.3 (54.1) | -13.62 (-31.26 to 4.03) |
| van den Boogaard, 2018[15](#_ENREF_15) | ICU patients at high risk of delirium | Haloperidol (Planned dose: 2mg), 732 | Placebo (Planned dose: 0.9% NaCl), 707 | Intravenous | Monomorphic ventricular tachycardia | 1 / 732 (0.13%) | 0 / 707 (0%) | 2.90 (0.12 to 71.01) |
| van den Boogaard, 2018[15](#_ENREF_15) | ICU patients at high risk of delirium | Haloperidol (Planned dose: 1mg), 350 | Placebo (Planned dose: 0.9% NaCl), 707 | Intravenous | Monomorphic ventricular tachycardia | 2 / 350 (0.57%) | 0 / 707 (0%) | 10.09 (0.49 to 209.51) |
| van den Boogaard, 2018[15](#_ENREF_15) | ICU patients at high risk of delirium | Haloperidol (Planned dose: 2mg),  | Placebo (Planned dose: 0.9% NaCl),  | Intravenous | Prolongation in the QTc interval Maximum QTc interval | Median of the maximum times, 465 (IQR, 446 to 483) | Median of the maximum times, 463 (IQR, 440 to 486) | 1 (-2 to 5) |
| van den Boogaard, 2018[15](#_ENREF_15) | ICU patients at high risk of delirium | Haloperidol (Planned dose: 1mg),  | Placebo (Planned dose: 0.9% NaCl),  | Intravenous | Prolongation in the QTc interval Maximum QTc interval | Median of the maximum times, 465 (IQR, 440 to 489) | Median of the maximum times, 463 (IQR, 440 to 486) |  |
| van den Boogaard, 2018[15](#_ENREF_15) | ICU patients at high risk of delirium | Haloperidol (Planned dose: 2mg), 732 | Placebo (Planned dose: 0.9% NaCl), 707 | Intravenous | Prolongation in the QTc interval Number of QTc time prolongations | 33 / 732 (4.5%) | 36 / 707 (5.1%) | 0.89 (0.56 to 1.40) |
| van den Boogaard, 2018[15](#_ENREF_15) | ICU patients at high risk of delirium | Haloperidol (Planned dose: 1mg), 350 | Placebo (Planned dose: 0.9% NaCl), 707 | Intravenous | Prolongation in the QTc interval Number of QTc time prolongations | 31 / 350 (8.9%) | 36 / 707 (5.1%) | 1.74 (1.09 to 2.76) |

| Author, year | Population | Intervention group, n | Control group, n | Route of administration | Outcome definition | n / N (%), intervention group | n / N (%), control group | Relative risk (95% CI) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Wang, 2012[16](#_ENREF_16) | Patients 65 or older admitted to the ICU after noncardiac surgery | Haloperidol (Planned dose: 0.5 mg followed by continuous infusion at a rate of 1 mL/hr (0.1 mg/hr haloperidol)), 229 | Placebo (Planned dose: Normal saline), 228 | Intravenous | Arrhythmia during study drug infusion | 6 / 229 (2.6%) | 5 / 228 (2.2%) | 1.19 (0.37 to 3.86) |
| Wang, 2012[16](#_ENREF_16) | Patients 65 or older admitted to the ICU after noncardiac surgery | Haloperidol (Planned dose: 0.5 mg followed by continuous infusion at a rate of 1 mL/hr (0.1 mg/hr haloperidol)),  | Placebo (Planned dose: Normal saline),  | Intravenous | Change of heart rate-corrected QT interval after study drug infusion,, ms, mean +/- SD | 1 (26%) | -1 (31%) | 2 (-3.2 to 7.2) |
| Wang, 2012[16](#_ENREF_16) | Patients 65 or older admitted to the ICU after noncardiac surgery | Haloperidol (Planned dose: 0.5 mg followed by continuous infusion at a rate of 1 mL/hr (0.1 mg/hr haloperidol)), 229 | Placebo (Planned dose: Normal saline), 228 | Intravenous | Prolongation in the QT interval Significant heart rate-corrected QT interval prolongation after study drug infusion | 4 / 229 (1.7%) | 5 / 228 (2.2%) | 0.80 (0.22 to 2.93) |

| Author, year | Population | Intervention group, n | Control group, n | Route of administration | Outcome definition | n / N (%), intervention group | n / N (%), control group | Relative risk (95% CI) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  Second-generation antipsychotic vs. placebo |   |   |   |   |   |   |   |   |
| Girard, 2010[4](#_ENREF_4) | > 18 years MV medical and surgical ICU patients | Ziprasidone (Planned dose: 40 Median dose: 113 (81-140), 30 | Placebo (Planned dose: 5ml), 36 | Oral | Prolongation in the QTc interval prolongation of the QTc > 500 ms while receiving study drug | 5 / 30 (%) | 3 / 36 (%) | 2.00 (0.52 to 7.69) |
| Girard, 2010[4](#_ENREF_4) | > 18 years MV medical and surgical ICU patients | Ziprasidone (Planned dose: 40 Median dose: 113 (81-140), 30 | Placebo (Planned dose: 5ml), 36 | Oral | Ventricular arrhythmias | 0 / 30 (%) | 0 / 36 (%) | Not calculable |
| Hakim, 2012[5](#_ENREF_5) | Patients 65 years or older experiencing subsyndromal delirium after on-pump cardiac surgery | Risperidone (Planned dose: 0.5mg), 51 | Placebo (Planned dose: given every 12 hours), 50 | Oral | Prolongation in the QT interval Abnormality | 0 / 51 (%) | 0 / 50 (%) | Not calculable |
| Larsen, 2010[9](#_ENREF_9) | Post-operative elderly joint replacement surgery patients | Olanzapine (Planned dose: 5mg), 196 | Placebo (Planned dose: 5mg), 204 | Oral | Arrhythmia | 2 / 196 (1%) | 1 / 204 (0.5%) | 2.08 (0.19 to 22.77) |
| Larsen, 2010[9](#_ENREF_9) | Post-operative elderly joint replacement surgery patients | Olanzapine (Planned dose: 5mg), 196 | Placebo (Planned dose: 5mg), 204 | Oral | Atrial Fibrillation | 6 / 196 (3.1%) | 3 / 204 (1.5%) | 2.08 (0.53 to 8.21) |
| Larsen, 2010[9](#_ENREF_9) | Post-operative elderly joint replacement surgery patients | Olanzapine (Planned dose: 5mg), 196 | Placebo (Planned dose: 5mg), 204 | Oral | CHF | 1 / 196 (0.5%) | 1 / 204 (0.5%) | 1.04 (0.07 to 16.53) |
| Prakanrattana, 2007[11](#_ENREF_11) | Elective Cardiac Surgery with cardiopulmonary bypass | Risperidone (Planned dose: 1mg), 63 | Placebo (Not applicable), 63 | Orally disintegrating tablet | Arrhythmia | 6 / 63 (9.5%) | 6 / 63 (9.5%) | 1.00 (0.34 to 2.93) |

| Author, year | Population | Intervention group, n | Control group, n | Route of administration | Outcome definition | n / N (%), intervention group | n / N (%), control group | Relative risk (95% CI) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  First-generation antipsychotic vs. second-generation antipsychotic |   |   |   |   |   |   |   |   |
| Girard, 2010[4](#_ENREF_4) | > 18 years MV medical and surgical ICU patients | Ziprasidone (Planned dose: 40 Median dose: 113 (81-140), 30 | Haloperidol (Planned dose: 5 Median dose: 15 (10.8-17), 35 | Oral | Prolongation in the QTc interval prolongation of the QTc > 500 ms while receiving study drug | 5 / 30 (%) | 2 / 35 (%) | 2.92 (0.61 to 13.96) |
| Girard, 2010[4](#_ENREF_4) | > 18 years MV medical and surgical ICU patients | Ziprasidone (Planned dose: 40 Median dose: 113 (81-140), 30 | Haloperidol (Planned dose: 5 Median dose: 15 (10.8-17), 35 | Oral | Ventricular arrhythmias | 0 / 30 (%) | 0 / 35 (%) | Not calculable |
|  First-generation antipsychotic vs. other |   |   |   |   |   |   |   |   |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Dexmedetomidine (Planned dose: 0.2–0.7 mcg/kg/h preceded by a loading dose of 1.0 ug/kg intravenously over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Arrhythmia | 3 / 30 (10%) | 2 / 30 (7%) | 1.50 (0.27 to 8.34) |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Dexmedetomidine (Planned dose: 0.2–0.7 mcg/kg/h preceded by a loading dose of 1.0 ug/kg intravenously over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Bradycardia (Heart rate decreased to <= 60 beats/min) | 2 / 30 (7%) | 8 / 30 (27%) | 0.25 (0.06 to 1.08) |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Dexmedetomidine (Planned dose: 0.2–0.7 mcg/kg/h preceded by a loading dose of 1.0 ug/kg intravenously over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Hypotension | 3 / 30 (10%) | 4 / 30 (13%) | 0.75 (0.18 to 3.07) |
| Abdelgalel, 2016[1](#_ENREF_1) | Adult intensive care patients of ASA physical status III and IV aged between 26 and 70 years | Haloperidol (Planned dose: 0.5– 2 mg/h preceded by a loading dose of 2.5 mg intravenously over 10 min if needed (if RASS > 2+), 30 | Dexmedetomidine (Planned dose: 0.2–0.7 mcg/kg/h preceded by a loading dose of 1.0 ug/kg intravenously over 10 min if needed (if RASS > 2+)), 30 | Intravenous | Prolongation in the QTc interval >500ms | 2 / 30 (7%) | 0 / 30 (0%) | 5.00 (0.25 to 99.95) |

ASA=American Society of Anesthesiologists; CI=confidence interval; ICU=intensive care unit; IQR=interquartile range; IV=intravenous; Mg=milligram; Mg=milligram; Ml/hr=milliliter per hour; Ml=milliliter; MV=mechanical ventilation; N=sample size; QT=Q and T wave interval; QTc=corrected QT interval; RASS=Richmond Agitation and Sedation Scale; SD=standard deviation; Ug/kg=microgram per kilogram