Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Pharmacological agents - prevention review

Study	*Participants*	*Interventions*
Aizawa 2002 RCT trial held in Japan. Setting: Hospital; ward/unit: ICU Funding :Unclear/ Not stated.	Inclusion criteria: Patients underwent resection of gastric or colorectal cancer. Exclusion criteria: Patients with liver cirrhosis, liver dysfunction, respiratory disturbance, mental disorders, visual impairment, patients requiring extended resection of other organs. Patient characteristics: age (range): 70-85 years., delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Comorbidities and medicines used Details: 26 M, 14 F; No details of delirium risk; no details of proportion of pts with dementia. Delirium assessment: Clinical interview; DSM-IV used to assess Post Op delirium. Other study comments: All patients were given epidural anesthesia for pain control for 2-3 days after surgery.	1) Diazepam + flunitrazepam drip infusion and pethidine for first 3 days (Benzodiazepines); duration: 3 days, follow up 7 days; frequency: OD; amount Diazepam 0.1 mg/kg IM + flunitrazepam 0.04 mg/kg drip infusion and 1 mg/kg pethidine (n=22). 2) No treatment given or placebo (No treatment); duration: 3 days, follow up 7 days; frequency: None; amount None (n=20).
Gamberini 2009 RCT trial held in Switzerland. Setting: Hospital; ward/unit: Surgical Funding :Grant from manufacturers.	Inclusion criteria: Patients recruited day before surgery btw Feb 2006 to July 2007. Age 65y or older and elective cardiac surgery with cardiopulmonary bypass. Exclusion criteria: Urgent or emergency surgery, previous cardiac surgery, cardiac surgery with non cardiac procdures (typically carotid endarterectomy), insufficient knowledge of German or sensory impairment interfereing with neuropsychological testing, MMSE score<15,psychi Patient characteristics: age (range): 74.3 years (estimated range: 68.5 to 80.3), delirium risk: High risk; cognitive impairment at baseline: Cognitive impairment deduced from scores. Comorbidities: Comorbidities: treated diabetes,COPD; Hypertension; medicines used Details: 77:36; delirium risk : assumed a high rate of delirium 65%; Mean MMSE score and range: 28 (23 to 30) indicating some patients may have had mild cognitive impairment. Delirium assessment: CAM; CAM assessment daily; CAM also used during patients stay in the ICU Other study comments: Exclusion continued: psychiatric illness requireing use of antidepressants or antipsychotics, preesisting neurologic deficits, previous or ongoing treatment with cholinesterase inhibitors, and known contraindications to rivastigmine.	1) administered with every meal as an odourless yellowish solution (Cholinesterase inhibitors); duration: The intervention was given the evening before surgery, three times per day every 8 hours thereafter until the evening of the sixth postoperative day; frequency: 3/day; amount 1.5 mg doses (n=56). 2) odourless yellowish solution (Placebo); duration: The placebo was given the evening before surgery, three times per day every 8 hours thereafter until the evening of the sixth postoperative day; frequency: 3/day; amount (n=57).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Pharmacological agents - prevention review

Study	*Participants*	*Interventions*
Kalisvaart 2005 RCT trial held in The Netherlands. Setting: Hospital; ward/unit: Surgical Funding :No funding.	Inclusion criteria: Men and women aged 70 years or older admitted for acute or elective hip surgery; patients had to be at intermediate or high risk for postoperative delirium; a maximum delay of surgery up to 72 hours Exclusion criteria: Patients with delirium at admission; no risk factors for postoperative delirium present at baseline; history of haloperidol allergy; use of cholinesterase inhibitors; parkinsonism, epilepsy, levodopa treatment, inability to interview Patient characteristics: age (range): 73-86 years, delirium risk: Mixed: High & Intermediate; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Comorbidities and medicines used Details: 80% female; 84% with an intermediate risk, and 16% with a high risk of delirium at baseline. Delirium assessment: CAM; Delirium severity was measured using the DRS-R-98; daily patients assessments using MMSE, DRS-R-98 and Digit Span test Other study comments: On average, both study groups included patients with minimal cognitive impairment, some visual impairment, and light dehydration.	1) Haloperidol (Typical antipsychotics); duration: Day of admission and up to 3 days postoperation; frequency: Three times daily; amount 1.5 mg (n=212). 2) Placebo (Placebo); duration: Day of admission and up to 3 days postoperation; frequency: Three times daily; amount Not stated (n=218).
Kaneko 1999 RCT trial held in Japan. Setting: Hospital; ward/unit: ICU Funding :Unclear/ Not stated.	Inclusion criteria: Men and women undergoing gastrointestinal surgery Exclusion criteria: Not stated Patient characteristics: age (range): 64-82 years, delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Details: 64% male; patients included those with ischaemic heart disease, hypertension, respiratory disease, diabetes mellitus, liver disease and premorbid cognitive impairment; most patients had partial gastroectomy. Delirium assessment: Not stated/Unclear; DSM-III-R diagnostic criteria; details not reported Other study comments: Drugs and method for postoperative pain control, hypoxia and infection were examined and not found to associated with the occurrence of postoperative delirium.	1) Haloperidol (Typical antipsychotics); duration: 5 days; frequency: Once daily intravenously; amount 5 mg (n=40). 2) Placebo (normal saline) (Placebo); duration: 5 days; frequency: Once daily; amount Not applicable (n=40).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Pharmacological agents - prevention review

Study	*Participants*	*Interventions*
Liptzin 2005 RCT trial held in USA. Setting: Hospital; ward/unit: Surgical Funding :Grant from manufacturers.	Inclusion criteria: Older population over 50 years without dementia undergoing total joint replacement surgery of the knee or hip. Exclusion criteria: Patients with GERD, or sick sinus syndrome excluded. Patient characteristics: age (range): 51-90 years., delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Comorbidities and medicines used Details: 34 M, F 46; No details of delirium risk; no details of proportion of pts with dementia. Delirium assessment: Clinical interview; Delirium Symptom Interview, Confusion Assessment Method, daily medical record, nursing-observation reviews, DSM-IV. Other study comments: Patients who exhibited symptoms of delirium were advised to double the dose of Doneperzil or placebo. Participants were given the study drug 14 days before the surgery, to achieve a steady state, and continued it for a further 14 days.	1) Donepezil at breakfast (Cholinesterase inhibitors); duration: 28 days; frequency: once daily; amount 5 mg (n=39). 2) Placebo (Placebo); duration: 28 days; frequency: once daily; amount none (n=41).
Moretti 2004 RCT trial held in Italy. Setting: Other; ward/unit: -------- Funding :Unclear/ Not stated.	Inclusion criteria: MMSE scores of at least 14; satisfied the DSM-IV criteria for dementia, and for vascular dementia with the NINDS-AIREN criteria. Exclusion criteria: Abnormal pressure hydrocephalus; previous psychiatric illness, central nervous system disorders, alcoholism; patients without reliable caregivers were also excluded. Patient characteristics: age (range): 65-80 years; mean age 76 years, delirium risk: Unclear or Not Stated; cognitive impairment at baseline: All patients with cognitive impairment. Comorbidities: dementia Details: 116 M, 130 F; Delirium risk: not stated;. Delirium assessment: CAM; Confusion Assessment Method; Other study comments: Comorbidities vascular dementia; assessed relative to time of randomisation at one year change data and two year endpoint data. Patients continued existing drug therapy e.g. antihypertensives, antidyslipidemic, antidiabetic drugs, etc	1) Rivastigmine titrated up to 6 mg/day after 16 weeks (Cholinesterase inhibitors); duration: 2 years; frequency: once; amount 3-6 mg/day (n=115). 2) Cardio-aspirin (usual medical care); duration: 2 years; frequency: once; amount 100 mg (n=115).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Pharmacological agents - prevention review

Study	*Participants*	*Interventions*
Prakkanrattana 2007 RCT trial held in Thailand. Setting: Hospital; ward/unit: ICU Funding :Grant- other.	Inclusion criteria: Cardiac patients over 40 years of age undergoing elective cardiopulmonary bypass surgery Exclusion criteria: Patients to undergo emergency surgery; patients admitted to ICU or who had tracheal intubation before surgery; patients experiencing preoperative delirium; patients with previous psychiatric problems Patient characteristics: age (range): 51 to 71 years, delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: 67% of the pts: coexisting diseases incl hypertension, diabetes mellitus, cerebrovascular accident, renal failure or atrial fibrillation Details: 59% men; 67% with coexisting disease including hypertension, diabetes mellitus, cerebrovascular accident, renal failure, atrial fibrillation. Delirium assessment: CAM; Diagnosed as the presence of 'acute onset or fluctuating course' and 'inattention' and either 'disorganised thinking' or 'altered level of consiousness'; patients interviewed twice daily in the ICU and once daily after being discharged from ICU Other study comments: Sedatives and anti-psychotics were not allowed before the evaluation; all delirium episodes occurred within the first three postoperative days.	1) Risperidone (oral tablet given sublingually) (Atypical antipsychotics); duration: First postoperative day; frequency: Administered once; amount 1 mg single dose given soon after recovery from anesthesia (n=63). 2) Placebo (antiseptic strip (Listerine) applied sublingually) (Placebo); duration: First postoperative day; frequency: Administered once; amount Not applicable (n=63).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Single component non pharmacological - hydration prevention review

Study	*Participants*	*Interventions*
Mentes 2003 Quasi RCT trial held in USA. Setting: Long term care; ward/unit: -------- Funding :Grant- other.	Inclusion criteria: 65 yr or older Exclusion criteria: Unstable congestive heart failure or diabetes, renal dis (creatinine >3.5mg/dL), hyponatraemia (Na<135mEq/L), terminally ill, acutely confused, UTI Patient characteristics: age (range): mean around 82yr, delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: not stated Details: 22 M: 27 F; at risk of dehydration; 11 pts with dementia; method of assessment of dementia not stated. Delirium assessment: MMSE; scored lower than baseline on MMSE and <25 on NEECHAM confusion scale Other study comments: Intervention pts:shorter LOS in LTC (23 mo vs. 95 mo, p<0.001), more at risk of confusion (NEECHAM 26.4 vs. 28.4, p=0.005), had more pts with dementia (9 vs. 2, p=0.02), & were more frail: FIM 79.4 vs. 112.2, p<0.001; range 0-126; higher=better function	1) Hydration (Hydration); duration: 8 weeks; frequency: several times; amount to individually calculated fluid goal (n=25). 2) Usual care (Usual care); duration: 8 weeks; frequency: not applicable; amount not applicable (n=24).
Robinson 2002 before and after study trial held in USA. Setting: Long term care; ward/unit: -------- Funding :Grant- other.	Inclusion criteria: not stated Exclusion criteria: not stated Patient characteristics: age (range): mean 83.5 years (range 66-97), delirium risk: Mixed: all risk categories; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: some patients had each of dementia, chronic heart failure, chronic renal disease, malnutrition, depression, cerebrovascular accident, diabetes Details: M:F 8:43; 41/51 had conditions putting them at higher risk of delirium; proportion of pts with dementia unclear. Delirium assessment: Not stated/Unclear; reported that 'episodes of mental status changes' were recorded, with no further details Other study comments: 41/51 had more than 4 medications, with 22 taking diuretics, 29 psychotropics, 28 laxatives, 1 steroids (all risk factors for dehydration)	1) hydration care package (care giver knowledgable about hydration, individualised plan for administering fluids, colourful beverage cart, choice of beverages) (Hydration); duration: 5 weeks; frequency: twice; amount 8 oz fluid (n=51). 2) N/a (----------); duration: ; frequency: ; amount (n=).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Single component non pharmacological - hydration prevention review

Study	*Participants*	*Interventions*
O'Keeffe 1996 RCT trial held in UK. Setting: Hospital; ward/unit: Medical Funding :Unclear/ Not stated.	Inclusion criteria: Patients admitted to an acute geriatric unit judged to require parenteral fluids for at least 48h because of mild dehyrdration or because of poor oral intake and who had cognitive impariment Exclusion criteria: Patients requiring IV medication, if more than 2l of fluids was administered during any 24h period, if there was clinical evidence for poor tissue perfusion or if the precise amount of fluid to be administered was critical (e.g. renal or heart failure) Patient characteristics: age (range): 83 years (75 to 91), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: All patients with cognitive impairment. Comorbidities: Comorbidities and medicines used: not reported Details: 23:37; Cognitive impariment defined as disorientation for time and place or a MMSE score of 20 or less. Delirium assessment: Not stated/Unclear; Delirium not assessed; Agitation assessed with modified Cohen-Mansfield Agitation Inventory Other study comments: The study compared the effectiveness and tolerability of two methods of delivering fluids; it was not concerned with preventing delirium. The study is therefore included as	1) Subcutaneous fluids administered in the infraclavicular, scapular, abdominal or thigh areas through a 21-gauge 'butterfly' cannula sited by a doctor; Hyaluronidase was not added to subcutaneous infusions (Hydration); duration: infused continously; frequency: ; amount Up to 2 litres of fluids /day permitted (n=30). 2) Intravenous fluids were administered through an 18- or 20-gauge cannula in the forearm veins. (Hydration); duration: infused continously; frequency: ; amount upto 2 litres of fluids/day permitted (n=30).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Single component non pharmacological music - prevention review

Study	*Participants*	*Interventions*
McCaffrey 2004 RCT trial held in USA. Setting: Hospital; ward/unit: Surgical Funding :Unclear/ Not stated.	Inclusion criteria: nonprobability convenient sample of postoperative elders (from tertiary care centre) who underwent elective hip or knee surgery, alert & oriented to provide consent & complete preoperative paperwork independently, able to hear music; 65 years or older Exclusion criteria: None reported Patient characteristics: age (range): 73 years (SD 5), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: not stated Details: not stated. Delirium assessment: Not stated/Unclear; chart numbers from nurses' computerised notes and checklists to determine number of episodes of confusion and signs of symptoms of delirium + score for readiness to ambulate Other study comments: nurses and family members were instructed and asked to turn on music when they walked into the othopaedic unit room; once awake & oriented, patients received same instructions	1) musical selection with bedside compact disc player automatically turned on + standard postoperative care (Music therapy); duration: from anaesthesia awakening time to the postoperative period -inclusive- until discharged; frequency: 3 times/day at most; amount at least 1 hr 3 times/day (n=not stated). 2) standard postoperative care (not described) (Usual care); duration: from anaesthesia awakening time to the postoperative period -inclusive- until discharged; frequency: n/a; amount n/a (n=not stated).
McCaffrey 2006 RCT trial held in USA. Setting: Hospital; ward/unit: Surgical Funding :Unclear/ Not stated.	Inclusion criteria: 65 years or older; postoperative elders who underwent elective hip or knee surgery, alert & oriented to provide consent & complete preoperative paperwork independently, able to hear music Exclusion criteria: None reported Patient characteristics: age (range): 75.7 years (SD 6); age range 59-82 years, delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: not stated Details: M 44(35.5%): F 80(64.5%); with hip surgery: 33% (40/120) & knee surgery: 67% (80/120). Delirium assessment: Not stated/Unclear; chart numbers from nurses' computerised notes and checklists to determine number of episodes of confusion and signs of symptoms of delirium + score for readiness to ambulate + distance ambulated (no. of feet ambulated in postop days) Other study comments: nurses and family members were instructed and asked to turn on music when they walked into the othopaedic unit room; once awake & oriented, patients received same instructions	1) musical selection with bedside compact disc player automatically turned on + standard postoperative care (Music therapy); duration: from the time awakening from anaesthesia until discharge; frequency: 4 times/day; amount at least 1 h, 4 times/day (n=62). 2) standard postoperative care (Usual care); duration: 3 days from the time awakening from anaesthesia to the postoperative period -inclusive- until discharged; frequency: n/a; amount n/a (n=62).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent prevention review

Study	*Participants*	*Interventions*
Gustafson 1991 Historical control trial held in Sweden. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: Patients 65 years or older; operated on for femoral neck fracture Exclusion criteria: Not stated Patient characteristics: age (range): 79 years (65-102), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Included cerebrovascular diseases, cardiovascular diseases, hypertension, diabetes, Parkinsons, renal failure, lung disease, infection; drugs reported Details: 74% female; 22% of pts with dementia in intervention group and 15% in control group; dementia diagnosed according to the DSM-III criteria. Delirium assessment: Clinical interview; DSM-III; Organic Brain Syndrome Scale; observed every day pre- and post-operatively; tested on days 1,3 and 7 after surgery Other study comments: The aim of this study was to determine if acute confusional state (ACS) (delirium) could be reduced by protecting the cerebral oxidative metabolism, mainly by improving cerebral perfusion and oxygenation	1) Geriatric-anesthesiologic intervention programme; surgical policy, pre-operative thrombosis prophylaxis; oxygen therapy; anaesthetic; post-op assessment and treatment (Multicomponent Prevention); duration: 8h to 7 days; frequency: ongoing; amount ongoing (n=103). 2) Usual pre- and post-operative hospital care (Usual care); duration: 8h to 7 days; frequency: ongoing; amount ongoing (n=111).
Harari 2007a Historical control trial held in UK. Setting: Hospital; ward/unit: Surgical Funding :Grant- other.	Inclusion criteria: Consecutively admitted orthopaedic patients (hip, knee and other replacement) aged 65 years or more Exclusion criteria: Not stated Patient characteristics: age (range): 75 years (68-81 years), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Rheumatoid arthritis, heart disease, atrial fibrillation, diabetes, renal impairment, hypertension, chronic lung disease, prostrate or bladder problem Details: 60% female; cognitive impairment and dementia not stated. Delirium assessment: Not stated/Unclear; Not stated Other study comments:	1) Proactive care of older people undergoing surgery ('POPS'); multidisciplinary preoperative comprehensive geriatric assessment service with post-operative follow-through (Multicomponent Prevention); duration: mean 11.5 days (hospital LoS); frequency: ongoing; amount ongoing (n=54). 2) Usual hospital care (Usual care); duration: mean 15.8 days (hospital LoS); frequency: ongoing; amount ongoing (n=54).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent prevention review

Study	*Participants*	*Interventions*
Inouye 1999 non-randomised controlled study trial held in USA. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: Patients admitted to one of three general-medicine units; at least 70 years old; no delirium at time of admission; intermediate or high risk at baseline Exclusion criteria: Inability to participate in interviews; profound aphasia; intubation or respiratory isolation; coma or terminal illness; hospital stay 48 hrs or less Patient characteristics: age (range): 74-86 (mean 80), delirium risk: Mixed: High & Intermediate; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Pneumonia; chronic lung disease; congestive heart failure, ischaemic heart disease, gastrointestinal disease, diabetes mellitus or metabolic disorder Details: 61% female; 6% in nursing home; 72% with intermediate risk of delirium and 28% with high risk; 11% with dementia using a modified Blessed Dementia Rating Scale (>2); MMSE scores ranged from 7 to 30, with 25% having a score of 20 or less. Delirium assessment: CAM; Other study comments: Other comorbidities: cancer, cerebrovascular disease, renal failure, anemia; medications not reported; visual and hearing impairment in 23% and 26% respectively ; Bogardus 2003: 6 month follow-up	1) Elder Life Program: (Multicomponent Prevention); duration: 7 days (median) in hospital; frequency: ; amount (n=426). 2) (Usual care); duration: 6.5 days (median) in hospital; frequency: ; amount (n=426).
Landefeld 1995 RCT trial held in USA. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: Patients 70 years or older admitted for general medical care Exclusion criteria: Patients admitted to intensive care, cardiology or other specialist unit Patient characteristics: age (range): 80 years (73-87), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Congestive heart failure, cancer, chronic lung disease, history of myocardial infarction, cerebrovascular disease, dementia Details: 67% female; mental status score was 16.8 (SD 3.9) in intervention group and 16.9 (SD 4.1) in the control group. Delirium assessment: MMSE; Mini-Mental State scale Other study comments: 1794 eligible patients; reasons for admission were change in mental status; cardiac problems, infection, pulmonary problems, gastrointestinal problems, diabetes mellitus, failure to thrive, or other problems	1) Acute Care for Elders: specially designed environment, patient-centred care, planning for discharge, and review of medical care (Multicomponent Prevention); duration: Admission to discharge; frequency: ongoing; amount ongoing (n=327). 2) Usual hospital care (Usual care); duration: Admission to discharge; frequency: ongoing; amount ongoing (n=324).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent prevention review

Study	*Participants*	*Interventions*
Lundstrom 2005 Quasi RCT trial held in Sweden. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: Patients 70 years or older; all patients included regardless of diagnosis Exclusion criteria: Not stated Patient characteristics: age (range): 74-87 years, delirium risk: Mixed: all risk categories; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Asthma, diabetes mellitus, myocardial infarction, heart failure, stroke, epilepsy, malignancies, infection and urinary infection; drugs reported Details: 56% female; 4.5% pts with dementia at baseline. Delirium assessment: MMSE; Patients assessed using the Organic Brain Syndrome Scale and the MMSE on days 1, 3, and 7 after admission; delirium according the DSM-IV criteria Other study comments: Staff education focused on assessment, prevention and treatment of delirium and on caregiver-patient interaction; reorganisation from a task-allocation care system to a patient-allocation system with individualised care; impaired hearing and vision	1) Education programme and reorganisation of nursing and medical care (Multicomponent Prevention); duration: 7 days; frequency: ; amount (n=200). 2) Usual hospital care organised in a task-allocation care system (----------); duration: 7 days; frequency: ; amount (n=200).
Marcantonio 2001 RCT trial held in USA. Setting: Hospital; ward/unit: Surgical Funding :Grant- other.	Inclusion criteria: Patients 65 years or older for primary surgical repair of hip fracture Exclusion criteria: Presence of metastatic cancer or other comorbid illnesses likely to reduce life expectancy to less than 6 months Patient characteristics: age (range): 70-88 years, delirium risk: ; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Not stated specifically; 39% in intervention group and 33% in the control group had high medical comorbidity (Charlson index >or=4) Details: 79% female; 40% pts with dementia at baseline (Blessed score >4). Delirium assessment: CAM; Individual symptoms using the Delirium Symptom Interview (DSI); severity of delirium using the Memorial Delirium Assessment Scale (MDAS); MMSE to assess cognitive function Other study comments: Intervention began preoperatively or 24 hours postoperatively; fracture included femoral neck, intertrochanteric or 'other'; overall adherence rate by the orthopaedics team was 77%; hearing/sight impairment not reported	1) Proactive geriatrics consultation; target recommendations based on a structured protocol (Multicomponent Prevention); duration: Median 5 days, IQR 2; frequency: daily visits; amount (n=62). 2) Usual care; management by orthopaedics team on a reactive rather than proactive basis (----------); duration: Median 5 days, IQR 2; frequency: ; amount (n=64).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent prevention review

Study	*Participants*	*Interventions*
Wanich 1992 non-randomised controlled study trial held in USA. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: All person aged 70 years or older admitted to hospital during the week Exclusion criteria: Patients transferred from another hospital unit; admitted for a short stay procedure (e.g. chemotherapy, transfusion); admitted only for terminal care Patient characteristics: age (range): mean age 77 years (SD 9.4), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Patients admitted for a number of conditions. Categories included cardiac, respiratory, infection, metabolic, neoplasm, cerebrovascular and other Details: approx 50% female; proportion with cognitive impairment not stated; cognitive impairment assessed using MMSE (score <24). Delirium assessment: Clinical interview; Diagnosis of delirium was established prospectively by a study psychiatrist using DSM-III criteria Other study comments: 352 eligible patients; consent was not received from 117 patients; 60% resided independently before admission; some contamination of interventions between two groups reported	1) Nursing interventions: education, orientation and communication, mobilisation, environmental modifications, medication management, discharge planning (Multicomponent Prevention); duration: 9 months; frequency: Assessed daily; amount ongoing (n=135). 2) Usual hospital care on a different ward (Usual care); duration: 9 months; frequency: ongoing; amount ongoing (n=100).
Wong 2005 Historical control trial held in Australia. Setting: Hospital; ward/unit: Medical Funding :Unclear/ Not stated.	Inclusion criteria: Osteoporotic hip fracture patients > 50 years of age admitted to an orthopaedic unit Exclusion criteria: Not stated Patient characteristics: age (range): 82 years (50-96), delirium risk: Unclear or Not Stated; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Vascular disease; diabetes; chronic lung disease; depression/anxiety; medications not stated Details: 72% female; cognitive status was assessed using the Abbreviated Mental Test (AMT); 32% in baseline group had a low mental test score (< 8/10) and 38% had a low mental test score post-intervention. Delirium assessment: CAM; Administered daily Other study comments: One of strategies included low dose haloperidol or lorazepam; Tramadol was used in the pain management strategy; during the intervention period, an average of 6 recommendations were given per patient; 90% recommendations were followed	1) Delirium education for hospital staff; recommendations by geriatric registrars (10 possible strategies) (Multicomponent Prevention); duration: 3 months; frequency: ongoing; amount ongoing (n=71). 2) Usual hospital care (Usual care); duration: 1 month; frequency: ongoing; amount ongoing (n=28).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Pharmacological agents - treatment review

Study	*Participants*	*Interventions*
Hu 2006 RCT trial held in China. Setting: Hospital; ward/unit: Unclear/ Not stated Funding :Unclear/ Not stated.	Inclusion criteria: Aged 65years or more; 'senile delirium' due to metabolic (68), toxic (47), structural (25) or infectious cause (35); delirium rating scale 12 or more; clinical global impression-severity of illness score 4 or more Exclusion criteria: severe mental disease, antipsychotic drug, angle-closure glaucome, paralytic ileus, substance abuse Patient characteristics: age (range): mean 74 years (65-99), delirium risk: ; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Comorbidities and medicines used not stated Details: 111 M: 64F; proportion of pts with dementia not stated. Delirium assessment: DSM IV; DRS Other study comments: Duration of delirium 30 min-17day.	1) Haloperidol (IM) (Typical antipsychotics); duration: 1 week; frequency: not stated; amount 2.5-10mg/day (n=75). 2) Olanzapine (orally or sublingually) (Atypical antipsychotics); duration: 1 week; frequency: not stated; amount 1.25-20mg/day (n=75).
Liu 2004 non-randomised controlled study trial held in Taiwan. Setting: Hospital; ward/unit: Mixed: Medical & Surgical Funding :Grant from manufacturers.	Inclusion criteria: patients in general wards examined by psychiatrists in liaison team & having diagnosis of delirium on DSM-IV criteria Exclusion criteria: not stated Patient characteristics: age (range): haloperidol 49.89 years(15-77); risperidone 67.88 years (40-85), delirium risk: ; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Comorbidities and medicines used not stated Details: 54M:23F; 3 in each group had post-operative delirium. Delirium assessment: DSM IV; patient was no longer considered delirious when did not meet DSM-IV criteria for 2 consecutive days Other study comments: retrospective, big difference in age groups between risperidone & haloperidol groups; range of aetiologies of delirium	1) Haloperidol (Typical antipsychotics); duration: mean 7.9 days (range 2-19 days); frequency: not stated; amount maximal daily dose 1.0-10.0mg (mean 4.25mg; initially IM then oral) (n=36). 2) Risperidone (Atypical antipsychotics); duration: mean 7.2 days (range 3-18 days); frequency: not stated; amount maximal daily dose 0.5-4.0mg (mean 1.17mg) (n=41).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Pharmacological agents - treatment review

Study	*Participants*	*Interventions*
Miyaji 2007 non-randomised controlled study trial held in Japan. Setting: Hospital; ward/unit: Unclear/ Not stated Funding :Unclear/ Not stated.	Inclusion criteria: Inpatients referred for treatment of delirium Exclusion criteria: previous or existing mental disease, alcohol or benzodiazepine withdrawal delirium, suspected dementia Patient characteristics: age (range): median 72.4 years(IQR 65-78 yr); group 3 (haloperidol injection) significantly younger, delirium risk: ; cognitive impairment at baseline: No patients with cognitive impairment. Comorbidities: Comorbidities and medicines used not stated Details: 179M:87F; no patients with dementia. Delirium assessment: DSM IV; DSM-IV criteria; duration of delirium from when psychiatrist 1st considered patient had delirium until when no longer met criteria Other study comments: Retrospective study with main outcome of adverse events; not all patients followed up & n's not given	1) Haloperidol (oral) (Typical antipsychotics); duration: up to 19 days; frequency: not stated; amount median initial dose 0.75mg (IQR 0.75-1.5); max 1.5 (0.75-3.0)mg (n=95). 2) Risperidone (Atypical antipsychotics); duration: up to 14 days; frequency: not stated; amount median initial dose 0.5mg (IQR 0.5-1.0); max 1.0 (0.5-2.0)mg (n=93).
Skrobik 2004 Quasi RCT trial held in Canada. Setting: Hospital; ward/unit: ICU Funding :Grant from manufacturers.	Inclusion criteria: DSM-IV delirium Exclusion criteria: Pregnant, antipsychotic drug within 10 days prior to hospital/ICU admission, Parkinson's disease, oropharyngeal dysfunction, prolonged QT interval, hepatic/renal/GI dysfunction, neuropsychiatric evaluation impossible (e.g. coma, stupor) Patient characteristics: age (range): mean around 65 years; significantly lower in the haloperidol group compared w/olanzapine (63 vs 67), delirium risk: ; cognitive impairment at baseline: Unclear or Not stated. Comorbidities: Comorbidities and medicines used Details: 53 M: 20F; predominantly surgical population. Delirium assessment: Clinical interview; ICDSC, then if 4 or more (or clinical diagnosis of delirium) confirmed using DSM-IV criteria Other study comments: Mostly surgical (48 elective; 21 urgent; 4 medical); no difference in rescue haloperidol; benzodiazepine, opiates (fentanyl) and other sedatives. Patients treated within 2h of diagnosis of delirium.	1) Haloperidol (Typical antipsychotics); duration: 5 days; frequency: 3 times; amount 2.5-5mg 8-hourly or 0.5-1mg if over 60 yr then titrated (n=45). 2) Olanzapine (Atypical antipsychotics); duration: 5 days; frequency: once; amount 5mg or 2.5mg if over 60 y then titrated (n=28).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent treatment review

Study	*Participants*	*Interventions*
Cole 1994 RCT trial held in Canada. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: 75 years or older, admitted to medical department, spoke English or French Exclusion criteria: CVA, admitted to ICU or cardiac monitoring unit, referred to oncology or geriatric service Patient characteristics: age (range): mean 85.5 years, delirium risk: ; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Comorbidities and medicines used Details: 31 M: 57F; 56% of pts in treatment group with dementia (not specified for controls); method of assessment of dementia DSM-III-R criteria (mainly Alzheimer's disease). Delirium assessment: CAM; 5 or more on SPMSQ (moderate to severe cognitive impairment) assessed with CAM Other study comments: Intervention:environment (not excess sensory input, medication not interrupting sleep), orientation (clock, calendar, glasses, hearing aid, interpreter), familiarity (objects from home, same staff), communication (clear, facing pt), activities (self care)	1) consultation by geriatrician or geriatric psychiatrist & follow up by liaison nurse (multicomponent); duration: 8 weeks; frequency: daily visits & management by protocol; amount not applicable (n=42). 2) 'regular medical care' (usual medical care); duration: 8 weeks; frequency: not stated; amount not applicable (n=46).
Cole 2002 RCT trial held in Canada. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: 65 years or older, admitted to medical department, spoke English or French Exclusion criteria: CVA, admitted to ICU or cardiac monitoring unit >48hrs, admitted to oncology or geriatric service, not resident on island on Montreal Patient characteristics: age (range): mean around 82 years, delirium risk: ; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Comorbidities and medicines used Details: 104 M: 123F; 58% of pts with dementia; method of assessment of dementia family member reported by Informant Questionnaire on Cognitive Decline in the Elderly. Delirium assessment: CAM; 3-9 errors on SPMSQ (moderate to severe cognitive impairment) or symptoms of delirium in nursing notes assessed with CAM Other study comments: Intervention:environment (not excess sensory input, medication not interrupting sleep), orientation (clock, calendar, glasses, hearing aid, interpreter), familiarity (objects from home, same staff), communication (clear, facing pt), activities (self care)	1) consultation by geriatrician or psychiatrist & follow up by liaison nurse (multicomponent); duration: 8 weeks; frequency: daily visits & management by protocol; amount not applicable (n=113). 2) 'regular medical care' (usual medical care); duration: 8 weeks; frequency: not stated; amount not applicable (n=114).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent treatment review

Study	*Participants*	*Interventions*
Milisen 2001 Cohort trial held in Belgium. Setting: Hospital; ward/unit: Surgical Funding :Mixed.	Inclusion criteria: traumatic fracture of proximal femur Exclusion criteria: multiple trauma, concussion, pathological fracture, surgery >72 hr after admission, aphasia, blindness, deafness, <9yr education Patient characteristics: age (range): median 81 years, delirium risk: ; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Comorbidities and medicines used Details: 23M:97F; many comorbidities; around 15% dementia assessed by MMSE. Delirium assessment: CAM; CAM on 1st, 3rd, 5th, 8th & 12th postoperative days Other study comments: duration of study unclear - measurements taken to day 12	1) nurse education; screening; antidelirium intervention; access to resource nurses/consultants; scheduled pain medication (multicomponent); duration: from admission to discharge; frequency: ongoing; amount ongoing (n=60). 2) usual nursing care prior to introduction of intervention (Usual care); duration: from admission to discharge; frequency: ongoing; amount ongoing (n=60).
Naughton 2005 Historical control trial held in USA. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: Patient aged 75 years or older; cognitively impaired and delirious that began in the emergency department and were moved to an acute geriatric unit Exclusion criteria: Patients in ICU or from a skilled nursing facility Patient characteristics: age (range): 81 years (75-87), delirium risk: ; cognitive impairment at baseline: All patients with cognitive impairment. Comorbidities: Comorbidities not stated; benzodiazepines, antidepressants, antihistamines, opiates, and neuroleptics Details: 65% female; proportion of pts with dementia not stated. Delirium assessment: CAM; further assessment details not stated Other study comments: A third cohort was evaluated at 9 months after the intervention (n=110); one of the objectives of the study was to change prescribing patterns in order to prevent and reduce delirium	1) Education and management of delirium on an acute geriatric unit (AGU) (multicomponent); duration: 4 months after intervention - patients measured on day 4 of hospitalisation; frequency: ongoing; amount ongoing (n=154). 2) Usual hospital care and prescription of psychotropic medications (Usual care); duration: baseline; measured 4 days after hospitalisation; frequency: ongoing; amount ongoing (n=110).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent treatment review

Study	*Participants*	*Interventions*
Naughton 2005 Historical control trial held in USA. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: All person aged 70 years or older admitted to hospital during the week Exclusion criteria: Patients in ICU or from a skilled nursing facility Patient characteristics: age (range): 81 years (75-87), delirium risk: ; cognitive impairment at baseline: All patients with cognitive impairment. Comorbidities: Comorbidities not stated; benzodiazepines, antidepressants, antihistamines, opiates, and neuroleptics Details: 65% female; proportion of pts with dementia not stated. Delirium assessment: CAM; further assessment details not stated Other study comments: A third cohort was evaluated at 9 months after the intervention (n=110); one of the objectives of the study was to change prescribing patterns in order to prevent and reduce delirium	1) Nursing interventions: education, orientation and communication, mobilisation, environmental modifications, medication management, discharge planning (multicomponent); duration: 4 months after intervention - patients measured on day 4 of hospitalisation; frequency: ongoing; amount (n=154). 2) Usual hospital care and prescription of psychotropic medications (Usual care); duration: ongoing; frequency: ongoing; amount (n=110).
Pitkala 2006 RCT trial held in Finland. Setting: Hospital; ward/unit: Medical Funding :Grant- other.	Inclusion criteria: less than 69 years Exclusion criteria: life expectancy <6months, inability to obtain informed consent from proxy <2days, admitted from permanent institutional care Patient characteristics: age (range): mean age 83 yr, delirium risk: ; cognitive impairment at baseline: Some patients with cognitive impairment. Comorbidities: Comorbidities and medicines used Details: 66 M: 128F; 31% of pts with dementia using Clinical Dementia Rating Scale, interview of proxies, DSM-IV criteria & medical records. Delirium assessment: CAM; If positive on CAM screening, physician confirmed diagnosis using DSM-IV criteria Other study comments: recognise delirium & underlying conditions; assessment & treatment (e.g. nutrition, review drugs), avoid neuroleptics, orientation, physio, Ca/vit D/other supplements, hip protectors, screen for treatable causes, cholinesterase inhibitor, discharge plan	1) Comprehensive assessment and treatment (see Study Comments) (multicomponent); duration: in hospital - follow up to 1 yr; frequency: not stated; amount not applicable (n=87). 2) Usual care (usual medical care); duration: in hospital - follow up to 1 yr; frequency: not stated; amount not applicable (n=87).

Appendix D: Included Studies: Pharmacological agents and Nonpharmacological interventions Prevention and Treatment

Multicomponent treatment review

Study	*Participants*	*Interventions*
Rahkonen 2001 Cohort trial held in Finland. Setting: Mixed; ward/unit: Medical Funding :Unclear/ Not stated.	Inclusion criteria: community-dwelling people >65yr admitted to hospital with delirium or delirium immediately after admission Exclusion criteria: severe underlying disorders (communication disorders, stroke, malignancy, alcoholism, major psychiatric disorder); surgical pts; ICU or cardiac unit; discharge <24hr Patient characteristics: age (range): 82 years (71-93), delirium risk: ; cognitive impairment at baseline: No patients with cognitive impairment. Comorbidities: Comorbidities and medicines used Details: 5M: 46F; no pts with dementia (prior diagnosis of dementia or symptoms or info from caregiver/relatives led to exclusion of patients with dementia); mild cognitive impairment included. Delirium assessment: Clinical interview; diagnosis based on DSM-III-R criteria Other study comments: control group matched on age & gender fulfilling same inclusion criteria but admitted in previous years. Follow up 3 yr; outcomes measured from official registers	1) support & counselling by nurse specialist working as case manager & rehabilitation at rehab centre (Multicomponent Prevention); duration: rehab 1 week per year; support throughout 3 yr; frequency: ongoing; amount ongoing (n=51). 2) standard aftercare (Usual care); duration: 3 yr; frequency: ongoing; amount ongoing (n=51).