

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted HR	1.1 (1.04, 1.15)	HR	age in years (of the patients with acute confusional stated, 47% were over 85 years, and 11% without ACS were over 85 years); mean 77 years (65-96)	Age: 77 years (65-96) Cognitive impairment: No patients with cognitive impairment; patients with established diagnosis of mental disease or already confused excluded. Sensory impairment: 31% visual and 39% hearing impairment. Medications: not stated	MV: age, gender, marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss; time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time,	Number key RFs: 4/4 (patients with dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium: 51/457 developed delirium
Leung 2007; prospective cohort study in 203 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery). QUALITY RATING: low	multivariate adjusted OR	1.08 (1, 1.16)	n=189	continuous: age in years. mean 72.5 (SD 5.9) years	Age: 72.5 years (SD5.9) Cognitive impairment: Some patients with cognitive impairment; Telephone Interview of Cognitive Status instrument (adapted from MMSE); measured preoperatively (mean score 33.0 +-3.2). Sensory impairment: not stated. Medications: Benzodiazepines, opioids	MV: allele, age, pain, education, 5 ADLs, 7 ADLs, a history of CNS disorders, alcohol intake, cognitive status, GDS score (0-2).	No.events/no. covariates = 29/10 = 3. Number key RFs: 2/4 (age, dementia). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 29/190 (15%) developed delirium that persisted for 2 days after surgery
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery). QUALITY RATING: biased	multivariate adjusted OR	1.09 (1.09, 1.1)		continuous: age in years	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynaecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	No.events/no. covariates = 3195/16 = 200. Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Santos 2004; prospective cohort study in 220 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: low	multivariate adjusted OR	1.1 (1.01, 1.19)	p=0.03	continuous: age in years (group with delirium: 32% were 60-70 years, 54% were 70-80 years and 14% were 80 years or older). Age in group without delirium: 51% were 60-70 years, 46% were 70-80 years and 3% were 80 years of age or older	Age: 66-78 years Cognitive impairment: No patients with cognitive impairment; MMSE (using a cut-off of 23). Sensory impairment: Severe hearing or vision impairment excluded. Medications: Diuretics, calcium channel blockers, beta blockers, ACE inhibitors, nitrates, H2 blockers, diazepam, midazolam	MV: Those included in final model were age, blood urea, cardiothoracic index greater than 0.5, hypertension, smoking, blood replacement (intraoperative), atrial fibrillation, pneumonia, blood balance on 2nd day after surgery	No.events/no. covariates = 74/36 = 2. Number key RFs: 3-4/4 (age; dementia + sens. imp excluded; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 74/220 (34%) developed delirium after surgery
Sheng 2006; prospective cohort study in 156 patients. Funding: Grant- other. Setting: Hospital; Medical ward . QUALITY RATING: low	multivariate adjusted OR	1.1 (1, 1.2)		continuous: age in years; mean 79.2 years (65-95 years)	Age: 79.2 years (65-95) Cognitive impairment: Some patients with cognitive impairment; MMSE; overall scores at one month were 23.4 +-6.0. Sensory impairment: 28/156 (18%) stroke patients with vision field loss. Medications: Anticholinergics	MV: age, dementia prestroke, haemorrhagic stroke, metabolic factor, ability to lift both arms, Glasgow Coma Scale Score less than 15, dysphagia, neglect, impaired vision, systolic blood pressure, diastolic blood pressure, one or more metabolic factors, urinary tract infection, urinary incontinence and faecal incontinence	No.events/no. covariates = 39/14 = 3. Number key RFs: 3/4 (not polypharmacy). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 39/156 (25%) had delirium within 72 hrs of stroke
Yildizeli 2005; retrospective cohort study in 432 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (thoracic surgery). QUALITY RATING: biased	multivariate adjusted OR	1.04 (0, 0)	CI's not reported	continuous: age in years; mean 51.7 years (18-86 years)	Age: 51.7 years (18 to 86) Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Aminophylline, antiarrhythmics, antibiotics, steroids, anihypertensives	UV & MV: (preoperative variables) age, sex, chronic disease, alcohol abuse, psychiatric problems, diabetes, cerebrovascular disease, chemotherapy, operation due to malignancy, urgent operation, (postoperative variables) respiratory insufficiency; abnormal serum chemistry values, operation time, LOS, length of ICU stay, sleep deprivation, hypertension, infection, blood transfusion, use of various drugs, immobilisation	No.events/no. covariates = 23/25 = 1. Number key RFs: 1/4 RFs (age). Number of pts with delirium at baseline: None; no. pts developing delirium: 23/432 (5%) developed postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Rudolph 2007; prospective cohort study in 1218 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery). QUALITY RATING: moderate	multivariate adjusted RR	1.1 (1, 1.1)		continuous: age in years. mean 68.9 (SD 5.9) years	Age: 68.9 years (SD 5.9) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean 27.8 (1.6) at baseline; various other neuropsychologic tests applied = mild cognitive impairment. Sensory impairment: not stated. Medications: not stated	MV: age, male, any tobacco exposure, diabetes, previous myocardial infarction, vascular surgery No.events/no. covariates = 99/6 = 16. Number key RFs: 2/4 (age; dementia constant). Dementia excluded; mild cog imp included. Number of pts with delirium at baseline: Not clear; no. pts developing delirium: cumulative incidence was 99/1161 (9%) in the 7-day postoperative period

risk factor vs comparator: age <50 vs age>70

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Bucerius 2004; prospective cohort study in 16184 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	0.22 (0.15, 0.31)	age below 50 years versus age 70 or more	Age in 4 categories: less than 50 years; 50 or more to less than 60 years; 60 or more to less than 70; compared to 70 or more as reference; older than 70y 33%	Age: 64.8 years (SD 10.4) Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: Cerebrovascular disease; atrial fibrillation; diabetes; peripheral vascular disease; left ventricular ejection fraction 30% or less; shock; urgent operation; operating time over 3 hours; haemofiltration; transfusion above 2L; beating heart surgery; age (35 variables in total - all not reported) Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 1354/16184 developed postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age > 65 vs age < 65

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Kazmierski 2006; prospective cohort study in 260 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: low	multivariate adjusted OR	4 (1.5, 10.4)	p=0.005	dichotomous: greater than or equal to 65 years versus less than 65 years (67% in group with delirium and 36% in non-delirious group); mean 62 years (25-81 years)	Age: 62 years (25-81) Cognitive impairment: Some patients with cognitive impairment; MMSE score equal to or less than 24; 53% in group with delirium and 16% in non-delirious group (preoperatively). Dementia excluded. Sensory impairment: not stated. Medications: Not stated	UV and MV: age, gender (male), cognitive impairment (MMSE equal to or less than 24), major depression, atrial fibrillation, peripheral vascular disease, history of cerebrovascular disease, serum urea (greater than 50 mg/dl), serum creatinine (greater than 1.2 mg/dh), use of heart pacemaker, ventricular arrhythmia, arterial hypertension, diabetes mellitus, prior myocardial infarction, NYHA greater than II, alcohol abuse No.events/no. covariates = 30/16 = 2. Number key RFs: 2/4 (age and cognitive impairment in analysis). Number of pts with delirium at baseline: None; no. pts developing delirium: 30/260 (12%) developed delirium

risk factor vs comparator: age >70 vs age < 60

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Hofste 1997; prospective cohort study in 321 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: moderate	multivariate adjusted OR	3.5 (1.4, 8.4)		Age 70 years or over compared with below 60 years; mean 62 years (29-83 years)	Age: 62 years (29-83) Cognitive impairment: Some patients with cognitive impairment; Mini Mental State Examination (MMSE) below 24 (out of 30). Sensory impairment: not stated. Medications: not stated	MV: Age, gender, lowest preoperative haemoglobin, abnormalities on electroencephalogram, mechanical ventilation on day 1 No.events/no. covariates = 44/5 = 9. Number key RFs: 2/4 (age; cognitive impairment constant). Number of pts with delirium at baseline: Probably no delirium; no. pts developing delirium: 44/321 (14%) patients developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age >80 vs age < 81

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Levkoff 1988; retrospective cohort study in 1285 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward	multivariate adjusted OR	no data	Not significant; data not reported	dichotomous: age 80 years or more versus less than 80 years; 46% older than 80 in group with delirium and 36% in comparison group	Age: not reported Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: sex, emergency or elective admission, age (80+), chronic renal disease, urinary tract infection, sodium, anion gap, creatinine, AST, albumin, calcium, TIBC, haemotocrit, WBC, PT, urine, and proteinuria Number key RFs: 1/4 key RFs (age). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 117 patients with delirium were included in the study and matched with 1,168 controls
Levkoff 1992; prospective cohort study in 325 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery). QUALITY RATING: moderate	multivariate adjusted OR	no data	not reported	dichotomous: 80 years and older versus less than 80 years (11.4% patients less than 80 years in the institution group); mean 81.4 (7.7) years	Age: 81.4 years (SD7.7) Cognitive impairment: Some patients with cognitive impairment; 24% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity No.events/no. covariates = 91/4 = 23. Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 34/325 (11%) with delirium at admission; no. pts developing delirium: 91/291 (31%) without prevalent delirium developed delirium. Analysis only for incident cases.
Levkoff 1992 community; prospective cohort study in 211 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery). QUALITY RATING: moderate	multivariate adjusted OR	5.4 (2.4, 12.3)		dichotomous: 80 years and older versus less than 80 years; mean 78.1 (6.8) years	Age: 78.1 years (SD 6.8) Cognitive impairment: Some patients with cognitive impairment; 14% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity No.events/no. covariates = 43/4 = 11. Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 8/211 (4%) with delirium at admission; no. pts developing delirium: Community setting (n=211); 43/211 (21%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age >80 vs age < 81

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Levkoff 1992 institution; prospective cohort study in 114 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery). QUALITY RATING: moderate	multivariate adjusted OR	0.87 (0.22, 3.3)		dichotomous: 80 years and older versus less than 80 years (11.4% patients less than 80 years in the institution group)	Age: 87.4 years (SD 7.7) Cognitive impairment: Some patients with cognitive impairment; 42% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity No.events/no. covariates = 48/4 = 12. Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 26/114 (23%) with delirium at admission; no. pts developing delirium: Institution (n=114) 48/114 (42%) developed delirium
Ranhoff 2006; prospective cohort study in 401 patients. Funding: Grant- other. Setting: Hospital; ICU ward	multivariate adjusted OR	1.3 (0.7, 2.3)		dichotomous: age in years (80 years or greater versus less than 80 years). 60-94 years; mean 78.1 (8.8) years	Age: 60-94 years; 78.1 years (SD 8.8) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score two weeks prior to admission to SICU was 19.1 (11.0). Sensory impairment: 116/401 (29%) with vision impairment; patient/close relative asjed if vision problems affecting daily activity. Medications: not stated	MV: age, dementia, vision impairment, history of heavy alcohol use, number of drugs taken, s-albumin, APS score, fitted bladder catheter Number key RFs: 4/4. Number of pts with delirium at baseline: 62/401(16%) within 24 hrs of admission; no. pts developing delirium: Cumulative delirium (117/401 (29%); 55/401 (16%) developed delirium during the SICU stay
Schor 1992; prospective cohort study in 291 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	5.22 (2.6, 10.46)		dichotomous: age greater than 80 years versus less than 80 years; 76% in group with delirium and 33% in group without delirium	Age: 80.5 years (SD 7.6) Cognitive impairment: Some patients with cognitive impairment; method not reported; 42% with prior cognitive impairment in the group with delirium and 10% in group without delirium. Sensory impairment: 33% with vision loss and 21% with hearing loss. Medications: Neuroleptics, narcotics, H2 blocker, digoxin, anticholinergics, benzodiazepine, steroids, nonsteroidal anti-inflammatory	MV: age (greater than 80), prior cognitive impairment, fracture on admission, patients from an institution, male sex, infection, pain (poorly controlled), neuroleptic use, and narcotic use Number key RFs: 3/4 key RFs (age, dementia, and possibly sensory impairment). Number of pts with delirium at baseline: Patients with delirium on admission were excluded; no. pts developing delirium: 91/291 (31%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age >81 vs age < 81

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Goldenberg 2006; prospective cohort study in 77 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (hip fracture surgery)	multivariate adjusted OR	5.1 (0.9, 26.8)		81.9 years (66-98)	Age: 81.9 years (66 to 98) Cognitive impairment: Some patients with cognitive impairment; MMSE and Set Test (poss high score 30 on both); 43 pts- mild dementia MMSE score >16. Mean MMSE= 21.6 (range 2-30); Mean ST score= 20.2 (1-30). Sensory impairment: not stated. Medications: Not stated	MV: multiple medications, low scores on cognitive tests (ST score<20; MMSE score <24), decreased albumin level (<3.5 g/dL), decreased hematocrit level (<33%), age >81 years	Number key RFs: 3/4 (not sens. imp). Number of pts with delirium at baseline: None; no. pts developing delirium: 37/77 patients had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age \geq 65 vs age $<$ 65

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Bohner 2003; prospective cohort study in 153 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: moderate	beta from regression (standardised)	1.37 (0, 0)	SE 0.468	dichotomous: 64 years or greater versus less than 64 years	Age: not stated Cognitive impairment: Unclear or Not stated; MMSE measured but number of patients with cognitive impairment not stated. Sensory impairment: visual 61% and hearing 24% impairment; assessment method not stated. Medications: not stated	MV: Supra-aortic occlusive disease; major amputation; hypercholesterolaemia; age; body length; depression; cognitive impairment (MMSE); colloid infusion; minimal potassium level	No.events/no. covariates = 60/9 = 7. Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: None; no. pts developing delirium: 60/153 developed delirium
Bohner 2003; prospective cohort study in 153 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: moderate	multivariate adjusted OR	3.03 (0, 0)	p=0.02; 95% CI not given	dichotomous: 64 years or greater versus less than 64 years	Age: not stated Cognitive impairment: Unclear or Not stated; MMSE measured but number of patients with cognitive impairment not stated. Sensory impairment: visual 61% and hearing 24% impairment; assessment method not stated. Medications: not stated	MV: Supra-aortic occlusive disease; major amputation; hypercholesterolaemia; age; body length; depression; cognitive impairment (MMSE); colloid infusion; minimal potassium level	No.events/no. covariates = 60/9 = 7. Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: None; no. pts developing delirium: 60/153 developed delirium
Caeiro 2004; prospective cohort study in 218 patients. Funding: Grant- other. Setting: Hospital; Stroke unit ward . QUALITY RATING: low	multivariate adjusted OR	2.4 (1, 5.8)		dichotomous: 65 years or older versus less than 65 years; mean 57 years (24-86 years)	Age: 57 years (24-86) Cognitive impairment: Some patients with cognitive impairment; Diagnosis of dementia or mild cognitive impairment and memory and another cognitive impairment with problems in activities of daily living, from proxy. Sensory impairment: not stated. Medications: not stated	MV: Medical complications, neglect (clinical sign in stroke), stroke type (intracerebral haemorrhage/subarachnoid haemorrhage/cerebral infarct), age	No.events/no. covariates = 29/4 = 7. Number key RFs: 1/4 (age). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 29/218 stroke patients had delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age \geq 75 vs age < 75

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	0 (0, 0)	Not significant; data not reported	dichotomous: 75 years or more versus less than 75 years; 82% in group with delirium and 68% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types Number key RFs: 3/4 key RFs (not polypharmacy). Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

risk factor vs comparator: age 50-59 vs age >70

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Bucerius 2004; prospective cohort study in 16184 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	0.34 (0.27, 0.43)		Age in 4 categories: less than 50 years; 50 or more to less than 60 years; 60 or more to less than 70; compared to 70 or more as reference category (32.5%)	Age: not stated Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: Cerebrovascular disease; atrial fibrillation; diabetes; peripheral vascular disease; left ventricular ejection fraction 30% or less; shock; urgent operation; operating time over 3 hours; haemofiltration; transfusion above 2L; beating heart surgery; age (35 variables in total - all not reported) Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 1354/16184 developed postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured incidence of delirium

risk factor vs comparator: age 60-69 vs age>70

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Bucerius 2004; prospective cohort study in 16184 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	0.6 (0.52, 0.68)		Age in 4 categories: less than 50 years; 50 or more to less than 60 years; 60 or more to less than 70; compared to 70 or more as reference category (32.5%)	Age: not stated Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: Cerebrovascular disease; atrial fibrillation; diabetes; peripheral vascular disease; left ventricular ejection fraction 30% or less; shock; urgent operation; operating time over 3 hours; haemofiltration; transfusion above 2L; beating heart surgery; age (35 variables in total - all not reported)	Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 1354/16184 developed postoperative delirium

Outcome measured duration of delirium

risk factor vs comparator: age as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Ely 2007; prospective cohort study in 53 patients. Funding: Mixed. Setting: Hospital; ICU ward (unclear/not stated surgery). QUALITY RATING: moderate	multivariate adjusted OR	1.02 (0.98, 1.06)	p=0.44	continuous: age in years; range 31-79	Age: 31-79 years Cognitive impairment: Some patients with cognitive impairment; Baseline dementia reported in 16% (7/44) patients; assessment using Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Sensory impairment: not stated. Medications: Lorazepam	MV: APOE4 allele (present/absent); age in years, Acute Physiology and Chronic Health Evaluation II score (continuous), coma days (continuous), sepsis/acute respiratory distress syndrome/pneumonia (dichotomous), lorazepam total dose (continuous)	No.events/no. covariates = 47/6 = 8. Number key RFs: 2/4 (age; polypharmacy constant). Number of pts with delirium at baseline: Not stated; no. pts developing delirium: 47/53 (89%) developed delirium at some point during the ICU stay

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Age

Outcome measured severity of delirium

risk factor vs comparator: age as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
McCusker 2001; prospective cohort study in 444 patients. Funding: Grant- other. Setting: Hospital; Medical ward . QUALITY RATING: low	multivariate adjusted mean	0.54	beta coefficient; SE 0.02 and p value 0.09	Mean age 83.3 years (SD 7.0). Patients were from an RCT in sample with delirium, and a prospective cohort study including delirious and non-delirious patients.	Age: 83.3 years (SD 7.0) Cognitive impairment: Some patients with cognitive impairment; Assessed with IQCODE with cut off score of 3.5 or more for dementia. Sensory impairment: 20% with visual/hearing impairment. Medications:	baseline delirium severity; age, dementia (present, missing), comorbidity, study group (x2), prevalent delirium, visual or hearing impairment, cumulative number of room changes, isolation, hospital unit (x5), length of follow up, stimulation level (x2), not in same room, single room, physical restraint, medical restraint, surroundings not well lit, noise/quiet, radio/TV on, no clock/watch, no calendar, no personal possessions, not wearing glasses, not using hearing aid, family absent No.events/no. covariates = 444/24 = 18. Number key RFs: 3 (not polypharmacy). Number of pts with delirium at baseline: Cases (with delirium; 326/444 (73%)) & controls; no. pts developing delirium: Unclear: measuring severity over time.

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Cognitive impairment

Outcome measured incidence of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Korevaar 2005; prospective cohort study in 126 patients. Funding: Industry study. Setting: Hospital; Medical ward. QUALITY RATING: low	multivariate adjusted HR	9.48 (2.27, 39.54)	multivariate adjusted HR; p<0.01	dichotomous: cognitive impairment assessed using IQCODE (patients with a mean score of 3.9 or more were considered to have dementia) 54/126 (43%)	Age: 79.1 years (SD 7.8) Cognitive impairment: Some patients with cognitive impairment; MMSE (score less than 24 indicating cognitive impairment); 69/126 (53%). Sensory impairment: not stated. Medications: Benzodiazepines, narcotic analgetics, corticosteroids, antihistaminics, and cholingergics (less high-risk drugs also reported)	MV: age, cognitive impairment, Katz ADL: 5-6, Katz ADL: 7 or greater, malignancy, gastrointestinal bleeding, electrolytes, urea, leucocytes, narcotic analgetics	No.events/no. covariates = 36/10 = 4. Number key RFs: 2/4 (age, dementia). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 36/129 (29%) had delirium within 48 hrs after admission; unclear if this was prevalent or incident
Bohner 2003; prospective cohort study in 153 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	28 (0, 0)	p=0.001; 95% CI not given	cognitive impairment measured by MMSE less than 25 points versus MMSE 25 points or more; patients with delirium 26.69 (2.85), no delirium 28.27 (1.71)	Age: not stated Cognitive impairment: Unclear or Not stated; MMSE measured but number of patients with cognitive impairment not stated. Sensory impairment: visual 61% and hearing 24% impairment. Medications: not stated	MV: Supra-aortic occlusive disease; major amputation; hypercholesterolaemia; age; body length; depression; cognitive impairment (MMSE); colloid infusion; minimal potassium level	Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: None; no. pts developing delirium: 60/153 developed delirium
Edlund 2001; prospective cohort study in 101 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery). QUALITY RATING: biased	multivariate adjusted OR	3.53 (2.16, 4.9)	p<0.001; (logistic regression analysis to predict pre-operative delirium)	Dementia diagnosed with DSM-IV criteria; 21/101 (21%) with dementia	Age: 79.5 years (65-102) Cognitive impairment: Some patients with cognitive impairment; Dementia diagnosed with DSM-IV criteria; prefracture mental state also assessed from interviews with relatives/ carers and medical records. Sensory impairment: visual (23%) or hearing (30%) impairment; assessment method not stated. Medications: Diuretics, benzodiazepines, analgesics, neuroleptics	MV: (preop analysis): male gender, dementia, Parkinson's disease, constipation, previous delirium, drugs with anticholinergic effect, neuroleptics, fractures; MV (post-op analysis): male gender, creatinine, perioperative bp falls (3 variables), depressed mood postop, pneumonia postop.	No.events/no. covariates = 19/8 = 2. Number key RFs: Preop: 2/4 (polypharmacy, dementia). Postop: none. Number of pts with delirium at baseline: 30/101 (30%) had preoperative delirium; no. pts developing delirium: 19/101 (19%) patients had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Cognitive impairment

Outcome measured incidence of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Furlaneto 2006; prospective cohort study in 103 patients. Funding: Unclear/ Not stated. Setting: Hospital; Medical ward (fracture neck of femur surgery). QUALITY RATING: biased	multivariate adjusted OR	3.04 (1.24, 7.41)		dichotomous: Blessed dementia questionnaire given to patient's caregiver (a score above 4 was considered indicative of previous dementia) 46/103 (45%)	Age: 71-90 years Cognitive impairment: Some patients with cognitive impairment; MMSE (mean scores 12.07 (9.04) in delirium group and 17.74 (8.78) in control group); 10-item clock drawing test (mean scores 3 (2.34) and 4.73 (3.10). Sensory impairment: not stated. Medications: Antidepressants, benzodiazepines, antiparkinsons	MV: dementia and ADL	No.events/no. covariates = 30/2 = 15. Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 17/103 (17%) had delirium at admission; no. pts developing delirium: 13/103 (13%) developed delirium
Goldenberg 2006; prospective cohort study in 77 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (hip fracture surgery). QUALITY RATING: moderate	multivariate adjusted OR	6.9 (1.2, 39.5)	MMSE score <24	Diagnosed according to DSM IV criteria and MMSE <24; 53/77 (69%) had dementia	Age: 81.9 years (66 to 98) Cognitive impairment: Some patients with cognitive impairment; MMSE and Set Test (poss high score 30 on both); 43 pts- mild dementia MMSE score >16. Mean MMSE= 21.6 (range 2-30); Mean ST score= 20.2 (1-30). Sensory impairment: not stated. Medications: Not stated	MV: multiple medications, low scores on cognitive tests (ST score<20; MMSE score <24), decreased albumin level (<3.5 g/dL), decreased hematocrit level (<33%), age >81 years	No.events/no. covariates = 37/6 = 6. Number key RFs: 3/4 (not sens. imp). Number of pts with delirium at baseline: None; no. pts developing delirium: 37/77 patients had postoperative delirium
Kazmierski 2006; prospective cohort study in 260 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	10.2 (3.7, 28.6)	MMSE <24, p<0.0001;	MMSE less than or equal to 24; 53% in group with delirium and 16% in non-delirious group (preoperatively)	Age: 62 years (25-81) Cognitive impairment: Some patients with cognitive impairment; MMSE score equal to or less than 24; 53% in group with delirium and 16% in non-delirious group (preoperatively). Sensory impairment: not stated. Medications: Not stated	UV & MV: age, gender (male), cognitive impairment (MMSE equal to or less than 24), major depression, atrial fibrillation, peripheral vascular disease, history of cerebrovascular disease, serum urea (greater than 50 mg/dl), serum creatinine (greater than 1.2 mg/dh), use of heart pacemaker, ventricular arrhythmia, arterial hypertension, diabetes mellitus, prior myocardial infarction, NYHA greater than II, alcohol abuse	Number key RFs: 2/4 (age and dementia). Number of pts with delirium at baseline: None; no. pts developing delirium: 30/260 (12%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Cognitive impairment

Outcome measured incidence of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Levkoff 1992 community; prospective cohort study in 211 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	11.9 (4.1, 34.1)		Dichotomous: 'preexisting cognitive impairment' (includes dementia); 14%	Age: 78.1years (SD 6.8) Cognitive impairment: Some patients with cognitive impairment; 14% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity	Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 8/211 (4%) with delirium at admission; no. pts developing delirium: Community setting (n=211); 43/211 (21%) developed delirium
Levkoff 1992 institution; prospective cohort study in 114 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	1.9 (0.73, 5)		Dichotomous: 'preexisting cognitive impairment' (includes dementia); 42%	Age: 87.4 years (SD 7.7) Cognitive impairment: Some patients with cognitive impairment; 42% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity	Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 26/114 (23%) with delirium at admission; no. pts developing delirium: Institution (n=114) 48/114 (55%) developed delirium
Pisani 2007; prospective cohort study in 304 patients. Funding: Grant- other. Setting: Hospital; ICU ward . QUALITY RATING: moderate	multivariate adjusted OR	6.3 (2.9, 13.8)	p<0.001;	dementia assessed using the short form of the Informant Questionnaire on Cognitive Decline in the Elderly (score greater than 3.3 = dementia) 94/304 (31%)	Age: 66-83 years Cognitive impairment: Some patients with cognitive impairment; baseline dementia assessed using IQCODE. Sensory impairment: 11% with vision impairment and 17% with hearing impairment; proxy reported. Medications: Benzodiazepine, narcotics	MV: nonwhite race, medicaid status, alcohol, a history of depression, dementia (score greater than 3.3), APACHE II score (mean) (scale), any impairment of ADL, medication use, admitting diagnosis, admitting physiologic variables, admitting laboratory data	No.events/no. covariates = 214/24 = 9. Number key RFs: 2/4 (dementia; polypharmacy constant). Number of pts with delirium at baseline: not clear; no. pts developing delirium: 214/304 (71%) developed delirium within first 48 hrs of ICU admission

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Cognitive impairment

Outcome measured incidence of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

Study name	Outcome	Sum stats (95%CI)	comments: risk factor details:	other details:	factors adjusted for in multivariate analysis	
Pompei 1994_Chicago; prospective cohort study in 432 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	2.14 (1.12, 4.12)	NO LONGER SIGNIFICANT when incident delirium only (results not given)	MMSE; for patients with less than high school education, the cut-off was 21, with HS cut-off was 23, college edu cut-off 24 points); 158/432 (37%) Age: 68-83 years Cognitive impairment: Some patients with cognitive impairment; MMSE. Sensory impairment: not stated. Medications: not stated	MV: cognitive impairment, number of MDCs, depression, alcoholism (total scores greater than or equal to 2 using the short form of the Michigan Alcoholism Screening test)	Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 21/432 (5%) had delirium within 72 hrs of adm; no. pts developing delirium: 64/432 (15%) had delirium overall (prevalent + incident)
Pompei 1994_Yale; prospective cohort study in 323 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	4.75 (2.71, 8.33)	NO LONGER SIGNIFICANT when incident delirium patients only were analysed	MMSE; for patients with less than high school education, the cut-off was 21, with HS cut-off was 23, college edu cut-off 24 points); 39% with impaired Age: mean 79.2 (6) years Cognitive impairment: Some patients with cognitive impairment; MMSE. Sensory impairment: not stated. Medications: not stated	MV: cognitive impairment, number of MDCs, depression, alcoholism (total scores greater than or equal to 2 using the short form of the Michigan Alcoholism Screening test)	Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 48/323 (15%) had delirium within 72 hrs of adm; no. pts developing delirium: 85/323 (26.3%) had delirium overall (prevalent + incident)
Ranhoff 2006; prospective cohort study in 401 patients. Funding: Grant- other. Setting: Hospital; ICU ward. QUALITY RATING: moderate	multivariate adjusted OR	11.5 (6.1, 20.1)	Patients with MMSE less than 18 and impaired ADL (Barthel Index less than 95) and/or IADL (impairment on one or more tasks) = probable; 119/401 (30%)	Age: 78.1years (60-94) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score two weeks prior to admission to SICU was 19.1 (SD 11.0). Sensory impairment: 116/401 (29%) with vision impairment; patient/close relative asked if vision problems affecting daily activity. Medications: not stated	MV: age, dementia, vision impairment, history of heavy alcohol use, number of drugs taken, s-albumin, APS score, fitted bladder catheter	No.events/no. covariates = 55/8 = 7. Number key RFs: 4/4. Number of pts with delirium at baseline: 62/401(16%) within 24 hrs of admission; no. pts developing delirium: Cumulative delirium (117/401 (29%); 55/401 (16%) developed delirium during the SICU stay

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Cognitive impairment

Outcome measured incidence of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Schor 1992; prospective cohort study in 291 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery). QUALITY RATING: moderate	multivariate adjusted OR	8.97 (3.99, 20.14)		dichotomous: history of prior cognitive impairment vs no history of prior cognitive impairment	Age: 80.5 years (SD 7.6) Cognitive impairment: Some patients with cognitive impairment; method not reported; 42% with prior cognitive impairment in the group with delirium and 10% in group without delirium. Sensory impairment: 33% with vision loss and 21% with hearing loss. Medications: Neuroleptics, narcotics, H2 blocker, digoxin, anticholinergics, benzodiazepine, steroids, nonsteroidal anti-inflammatory	MV: age (greater than 80), prior cognitive impairment, fracture on admission, patients from an institution, male sex, infection, pain (poorly controlled), neuroleptic use, and narcotic use	No.events/no. covariates = 91/9 = 10. Number key RFs: 3/4 key RFs (age, dementia, and possibly sensory impairment). Number of pts with delirium at baseline: Patients with delirium on admission were excluded; no. pts developing delirium: 91/291 (31%) developed delirium
Sheng 2006; prospective cohort study in 156 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted OR	5.7 (11.3, 24.9)	dementia was not significant in univariate analysis (p=0.175)	dichotomous: pre-stroke dementia (method not stated); 12/156 (8%)	Age: 65-95 years (mean 80) Cognitive impairment: Some patients with cognitive impairment; MMSE; overall scores at one month were 23.4 +-6.0. Sensory impairment: 28/156 (18%) stroke patients with vision field los. Medications: Anticholinergics	MV: age, dementia prestroke, hemorrhagic stroke, metabolic factor, ability to lift both arms, Glasgow Coma Scale Score less than 15, dysphagia, neglect, impaired vision, systolic blood pressure, diastolic blood pressure one or more metabolic factors, urinary tract infection, urinary incontinence and faecal incontinence	Number key RFs: 3/4 (not polypharmacy). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 39/156 (25%) had delirium within 72 hrs of stroke
Veliz-Reissmuller 2007; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	11.3 (2.7, 47.7)	MMSE score <28	Preoperative MMSE score (up to 28 points versus greater than or equal to 29 points); 11/107 (10%) with ≤28 points	Age: 65-78 years Cognitive impairment: Some patients with cognitive impairment; MMSE; the median score was 29 (17-30) in the delirium group and 30 (27-30) in the non-delirium group. Sensory impairment: not stated. Medications: not stated	MV: age, alcohol consumption, memory complaints, CABG- valve versus CABG, valve versus CABG, preoperative MMSE score (less than or equal to 28 versus greater than or equal to 29 points)	Number key RFs: 3/4 (age and cognitive impairment; polypharmacy constant). Number of pts with delirium at baseline: not clear; no. pts developing delirium: 25/107 (23%) developed delirium postoperatively

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Cognitive impairment

Outcome measured incidence of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	2.82 (1.19, 6.63)	MMSE<24	dichotomous: cognitive impairment (MMSE score less than 24); 63% in group with delirium and 26% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure) of 18 or more, depressive symptoms, six or fewer social supports, fewer support types Number key RFs: 3/4 key RFs (not polypharmacy). Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

Outcome measured severity of delirium

risk factor vs comparator: cognitive impairment vs no cognitive impairment

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
McCusker 2001; prospective cohort study in 444 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted mean	1.13 (0, 0)	beta coefficient; SE 0.28 and p value <0.01	59.5% with dementia and 13.1% scores unavailable	Age: 83.3 years (SD 7.0) Cognitive impairment: Some patients with cognitive impairment; Assessed with IQCODE with cut off score of 3.5 or more for dementia. Sensory impairment: 20% with visual/hearing impairment. Medications:	baseline delirium severity; age, dementia (present, missing), comorbidity, study group (x2), prevalent delirium, visual or hearing impairment, cumulative number of room changes, isolation, hospital unit (x5), length of follow up, stimulation level (x2), not in same room, single room, physical restraint, medical restraint, surroundings not well lit, noise/quiet, radio/TV on, no clock/watch, no calendar, no personal possessions, not wearing glasses, not using hearing aid, family absent, Number key RFs: 3 (not polypharmacy). Number of pts with delirium at baseline: Cases (with delirium; 326/444 (73%)) & controls; no. pts developing delirium: Unclear: measuring severity over time.

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Gender

Outcome measured incidence of delirium

risk factor vs comparator: men vs women

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Edlund 2001; prospective cohort study in 101 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted OR	- 1.419 (- 0.274, - 2.564)	preop analysis (THIS IS cross sectional)	male gender; 28% male	Age: 79.5 years (65-102) Cognitive impairment: Some patients with cognitive impairment; Dementia diagnosed with DSM-IV criteria; prefracture mental state also assessed from interviews with relatives/ carers and medical records. Sensory impairment: visual (23%) or hearing (30%) impairment. Medications: Diuretics, benzodiazepines, analgesics, neuroleptics	MV: (preop analysis): male gender, dementia, Parkinson's disease, constipation, previous delirium, drugs with anticholinergic effect, neuroleptics, fractures; MV (post-op analysis): male gender, creatinine, perioperative bp falls (3 variables), depressed mood postop, pneumonia postop.	Number key RFs: 2/4 (polypharmacy, dementia). Number of pts with delirium at baseline: 30/101 (30%) had preoperative delirium; no. pts developing delirium: 19/101 (19%) patients had postoperative delirium
Kazmierski 2006; prospective cohort study in 260 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	no data	not significant; data not reported in final model	dichotomous: male (73% in group with delirium and 77% in non-delirious group)	Age: 62 years (25-81) Cognitive impairment: Some patients with cognitive impairment; MMSE score equal to or less than 24; 53% in group with delirium and 16% in non-delirious group (preoperatively). Sensory impairment: not stated. Medications: Not stated	UV and MV: age, gender (male), cognitive impairment (MMSE equal to or less than 24), major depression, atrial fibrillation, peripheral vascular disease, history of cerebrovascular disease, serum urea (greater than 50 mg/dl), serum creatinine (greater than 1.2 mg/dh), use of heart pacemaker, ventricular arrhythmia, arterial hypertension, diabetes mellitus, prior myocardial infarction, NYHA greater than II, alcohol abuse	Number key RFs: 2/4 (age and dementia). Number of pts with delirium at baseline: None; no. pts developing delirium: 30/260 (12%) developed delirium
Levkoff 1988; retrospective cohort study in 1285 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward . QUALITY RATING: biased	multivariate adjusted OR	no data	Not significant; data not reported	dichotomous: sex; 35% male is group with delirium and 42% male in comparison group	Age: not reported Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: sex, emergency or elective admission, age (80+), chronic renal disease, urinary tract infection, sodium, anion gap, creatinine, AST, albumin, calcium, TIBC, haematocrit, WBC, PT, urine, and proteinuria	No.events/no. covariates = 117/18 = 6. Number key RFs: 1/4 key RFs (age). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 117 patients with delirium were included in the study and matched with 1,168 controls

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Gender

Outcome measured incidence of delirium

risk factor vs comparator: men vs women

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Levkoff 1992; prospective cohort study in 325 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	1.36 (0.64, 2.9)		dichotomous: 67% female	Age: 81.4 years (SD 7.7) Cognitive impairment: Some patients with cognitive impairment; 24% with preexisting cognitive impairment; assessment methods not reported. Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, presence or absence of preexisting cognitive impairment, and illness severity Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 34/325 (11%) with delirium at admission; no. pts developing delirium: 91/325 (31%) developed delirium.
Levkoff 1992 community; prospective cohort study in 211 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	1.4 (0.63, 3.3)		dichotomous: 65% female	Age: 78.1 years (SD 6.8) Cognitive impairment: Some patients with cognitive impairment; 14% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 8/211 (4%) with delirium at admission; no. pts developing delirium: Community setting (n=211); 43/211 (21%) developed delirium
Levkoff 1992 institution; prospective cohort study in 114 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	4.9 (1.6, 15.3)		dichotomous: 71% female	Age: 87.4 years (SD 7.7) Cognitive impairment: Some patients with cognitive impairment; 42% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 26/114 (23%) with delirium at admission; no. pts developing delirium: Institution (n=114) 48/114 (55%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Gender

Outcome measured incidence of delirium

risk factor vs comparator: men vs women

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.71 (1.59, 1.86)		dichotomous: male versus female (50% male in entire sample)	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium
Schor 1992; prospective cohort study in 291 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	2.4 (1.19, 4.84)		dichotomous: male versus female; 40% male in group with delirium and 30% in group without delirium	Age: 80.5 years (SD 7.6) Cognitive impairment: Some patients with cognitive impairment; method not reported; 42% with prior cognitive impairment in the group with delirium and 10% in group without delirium. Sensory impairment: 33% with vision loss and 21% with hearing loss. Medications: Neuroleptics, narcotics, H2 blocker, digoxin, anticholinergics, benzodiazepine, steroids, nonsteroidal anti-inflammatory	MV: age (greater than 80), prior cognitive impairment, fracture on admission, patients from an institution, male sex, infection, pain (poorly controlled), neuroleptic use, and narcotic use	Number key RFs: 3/4 key RFs (age, dementia, and possibly sensory impairment). Number of pts with delirium at baseline: Patients with delirium on admission were excluded; no. pts developing delirium: 91/291 (31%) developed delirium
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	0 (0, 0)	Not significant; data not reported	dichotomous: male versus female; 59% in group with delirium and 41% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types	Number key RFs: 3/4 key RFs (not polypharmacy). Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Gender

Outcome measured incidence of delirium

risk factor vs comparator: women vs men

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Hofste 1997; prospective cohort study in 321 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	2.5 (1.3, 4.9)		female versus male; 27% female	Age: 62 years (29-83) Cognitive impairment: Some patients with cognitive impairment; Mini Mental State Examination (MMSE) below 24 (out of 30). Sensory impairment: not stated. Medications: not stated	MV: Age, gender, lowest preoperative haemoglobin, abnormalities on electroencephalogram, mechanical ventilation on day 1 Number key RFs: 2/4 (age; cognitive impairment constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 44/321 (14%) patients developed delirium

Risk factor: Continence

Outcome measured incidence of delirium

risk factor vs comparator: incontinence vs no incontinence

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Sheng 2006; prospective cohort study in 156 patients. Funding: Grant- other. Setting: Hospital; Medical ward	univariate analysis OR	3.02 (1.27, 7.21)	p=0.13; CIs calculated from raw data	dichotomous: urinary incontinence (27/156; 17%)	Age: 80 years (65-95) Cognitive impairment: Some patients with cognitive impairment; MMSE; overall scores at one month were 23.4 +-6.0. Sensory impairment: 28/156 (18%) stroke patients with vision field los. Medications: Anticholinergics	MV: age, dementia prestroke, hemorrhagic stroke, metabolic factor, ability to lift both arms, Glasgow Coma Scale Score less than 15, dysphagia, neglect, impaired vision, systolic blood pressure, diastolic blood pressure one or more metabolic factors, urinary tract infection, urinary incontinence and faecal incontinence Number key RFs: . Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 39/156 (25%) had delirium within 72 hrs of stroke

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Dehydration

Outcome measured incidence of delirium

risk factor vs comparator: urea as continuous variable

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Korevaar 2005; prospective cohort study in 126 patients. Funding: Industry study. Setting: Hospital; Medical ward	multivariate adjusted HR	1.1 (1.02, 1.18)	multivariate adjusted HR; p<0.01	continuous: urea (mmol/L) (nitrogen concentration as a measure of dehydration); 15.9 and 10.6 mmol/l with and without delirium respectively	Age: 79.1 years (SD7.8) Cognitive impairment: Some patients with cognitive impairment; MMSE (score less than 24 indicating cognitive impairment); 69/126 (53%). Sensory impairment: not stated. Medications: Benzodiazepines, narcotic analgetics, corticosteroids, antihistaminics, and cholingergics (less high-risk drugs also reported)	MV: age, cognitive impairment, Katz ADL: 5-6, Katz ADL: 7 or greater, malignancy, gastrointestinal bleeding, electrolytes, urea, leucocytes, narcotic analgetics Number key RFs: 2/4 (age, dementia). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 36/129 (29%) had prevalent delirium within 48 hrs after admission
Santos 2004; prospective cohort study in 220 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	1.03 (1.01, 1.05)	p=0.01	continuous: blood urea level (range 15-127 mg/dL)	Age: 66-78 years Cognitive impairment: No patients with cognitive impairment; MMSE (using a cut-off of 23). Sensory impairment: Severe hearing or vision impairment excluded. Medications: Diuretics, calcium channel blockers, beta blockers, ACE inhibitors, nitrates, H2 blockers, diazepam, midozalam	MV: Those included in final model were age, blood urea, cardiothoracic index greater than 0.5, hypertension, smoking, blood replacement (intraoperative), atrial fibrillation, pneumonia, blood balance on 2nd day after surgery Number key RFs: 3-4/4 (age; dementia + sens. imp excluded; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 74/220 (34%) developed delirium after surgery

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Dehydration

Outcome measured incidence of delirium

risk factor vs comparator: urea > 50 mg/dl vs urea < 50mg/dl

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Kazmierski 2006; prospective cohort study in 260 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	no data	not significant; no data in final model	dichotomous: serum urea concentration greater than 50 mg/dL; 21/260 (8%)	Age: 62 years (25-81) Cognitive impairment: Some patients with cognitive impairment; MMSE score equal to or less than 24; 53% in group with delirium and 16% in non-delirious group (preoperatively). Sensory impairment: not stated. Medications: Not stated	UV and MV: age, gender (male), cognitive impairment (MMSE equal to or less than 24), major depression, atrial fibrillation, peripheral vascular disease, history of cerebrovascular disease, serum urea (greater than 50 mg/dl), serum creatinine (greater than 1.2 mg/dl), use of heart pacemaker, ventricular arrhythmia, arterial hypertension, diabetes mellitus, prior myocardial infarction, NYHA greater than II, alcohol abuse Number key RFs: 2/4 (age and dementia). Number of pts with delirium at baseline: None; no. pts developing delirium: 30/260 (12%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Dehydration

Outcome measured incidence of delirium

risk factor vs comparator: urea nitrogen:creatinine >18 vs urea nitrogen:creatinine < 18

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Pisani 2007; prospective cohort study in 304 patients. Funding: Grant- other. Setting: Hospital; ICU ward	multivariate adjusted OR	no data	not significant; no data	148/214 (69%) patients with delirium, and 54/90 (60%) patients without delirium, had a ratio of serum urea nitrogen to creatinine greater than 18.	Age: 66-83 years Cognitive impairment: Some patients with cognitive impairment; baseline dementia assessed using IQCODE. Sensory impairment: 11% with vision impairment and 17% with hearing impairment; proxy reported. Medications: Benzodiazepine, narcotics	MV: nonwhite race, medicaid status, alcohol, a history of depression, dementia (score greater than 3.3), APACHE II score (mean) (scale), any impairment of ADL, medication use, admitting diagnosis, admitting physiologic variables, admitting laboratory data	Number key RFs: 2/4 (dementia; polypharmacy constant). Number of pts with delirium at baseline: not clear; no. pts developing delirium: 214/304 (71%) developed delirium within first 48 hrs of ICU admission
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	2.02 (0.59, 4.6)		dichotomous: abnormal blood urea nitrogen/creatinine ratio of 18 or more; 67% in group with delirium and 39% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types	Number key RFs: 3/4 key RFs (not polypharmacy). Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Electrolyte disturbance

Outcome measured incidence of delirium

risk factor vs comparator: electrolyte abnormality vs no electrolyte abnormality

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Yildizeli 2005; retrospective cohort study in 432 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (thoracic surgery)	multivariate adjusted OR	3.01 (0, 0)	CIs not reported	Sodium less than 130 or greater than 150 meq/L, potassium less than 3.0, or greater than 6 meq/L, or glucose less than 60 or greater than 300 mg/dL	Age: 18-86 years (mean 51.7) Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Aminophylline, antiarrhythmics, antibiotics, steroids, antihypertensives	UV & MV: (preoperative variables) age, sex, chronic disease, alcohol abuse, psychiatric problems, diabetes, cerebrovascular disease, chemotherapy, operation due to malignancy, urgent operation, (postoperative variables) respiratory insufficiency; abnormal serum chemistry values, operation time, LOS, length of ICU stay, sleep deprivation, hypertension, infection, blood transfusion, use of various drugs, immobilisation	Number key RFs: 1/4 RFs (age). Number of pts with delirium at baseline: None; no. pts developing delirium: 23/432 (5%) developed postoperative delirium
Zakriya 2002; prospective cohort study in 168 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery). QUALITY RATING: low	multivariate adjusted OR	2.4 (1.1, 5.3)		dichotomous: abnormal serum sodium (Na+) (below 135 or above 148 mEq/L); 22%	Age: 50-98 years Cognitive impairment: Unclear or Not stated; Dementia excluded.. Sensory impairment: not stated. Medications: not stated	MV: normal white blood cell count, abnormal serum Na+, ASA class greater than II, history of illness (3 : coronary artery disease, congestive heart failure, atrial fibrillation)	No.events/no. covariates = 47/6 = 8. Number key RFs: 1/4 (dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium: 47/168 (28%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Depression

Outcome measured incidence of delirium

risk factor vs comparator: depression vs no depression

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Bohner 2003; prospective cohort study in 153 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	2.43 (0, 0)	SE=0.48, p=0.0; 95% CI not given	Hamilton depression scale greater than 8 points; patients with delirium 8.16 (5.50), no delirium 5.32 (5.52)	Age: not stated Cognitive impairment: Unclear or Not stated; MMSE measured but number of patients with cognitive impairment not stated. Sensory impairment: visual 61% and hearing 24% impairment. Medications: not stated	MV: Supra-aortic occlusive disease; major amputation; hypercholesterolaemia; age; body length; depression; cognitive impairment (MMSE); colloid infusion; minimal potassium level Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: None; no. pts developing delirium: 60/153 developed delirium;
Edlund 2001; prospective cohort study in 101 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted OR	no data	not significant; no data reported.	not defined; 11/101 (11%)	Age: 79.5 years (65-102) Cognitive impairment: Some patients with cognitive impairment; Dementia diagnosed with DSM-IV criteria; prefracture mental state also assessed from interviews with relatives/ carers and medical records. Sensory impairment: visual (23%) or hearing (30%) impairment. Medications: Diuretics, benzodiazepines, analgesics, neuroleptics	MV: (preop analysis): male gender, dementia, Parkinson's disease, constipation, previous delirium, drugs with anticholinergic effect, neuroleptics, fractures; MV (post-op analysis): male gender, creatinine, perioperative bp falls (3 variables), depressed mood postop, pneumonia postop. Number key RFs: 2/4 (polypharmacy, dementia). Number of pts with delirium at baseline: 30/101 (30%) had preoperative delirium; no. pts developing delirium: 19/101 (19%) patients had postoperative delirium
Kazmierski 2006; prospective cohort study in 260 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	6.3 (1.4, 29.7)	p=0.02	dichotomous: major depression (not defined) 13% in group with delirium and 5% in non-delirium group	Age: 62 years (25-81) Cognitive impairment: Some patients with cognitive impairment; MMSE score equal to or less than 24; 53% in group with delirium and 16% in non-delirious group (preoperatively). Sensory impairment: not stated. Medications: Not stated	UV and MV: age, gender (male), cognitive impairment (MMSE equal to or less than 24), major depression, atrial fibrillation, peripheral vascular disease, history of cerebrovascular disease, serum urea (greater than 50 mg/dl), serum creatinine (greater than 1.2 mg/dh), use of heart pacemaker, ventricular arrhythmia, arterial hypertension, diabetes mellitus, prior myocardial infarction, NYHA greater than II, alcohol abuse Number key RFs: 2/4 (age and dementia). Number of pts with delirium at baseline: None; no. pts developing delirium: 30/260 (12%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Depression

Outcome measured incidence of delirium

risk factor vs comparator: depression vs no depression

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Pompei 1994_Chicago; prospective cohort study in 432 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery). QUALITY RATING: low	multivariate adjusted OR	3.19 (1.65, 6.17)		5 or more points using the short form of the Yesavage Geriatric Depression scale was considered indicative of depression; 41% and 17% with depression	Age: 68-83 years Cognitive impairment: Some patients with cognitive impairment; MMSE; for patients with less than high school education, the cut-off was 21, with HS cut-off was 23, college edu cut-off 24 points); 158/432 (37%). Sensory impairment: not stated. Medications: not stated	MV: cognitive impairment, number of major diagnostic categories, depression, alcoholism (total scores greater than or equal to 2 using the short form of the Michigan Alcoholism Screening test)	No.events/no. covariates = 64/4 = 16. Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 21/432 (5%) had delirium within 72 hrs of admis; no. pts developing delirium: 64/432 (15%) had delirium overall (prevalent + incident)
Pompei 1994_Yale; prospective cohort study in 323 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery). QUALITY RATING: biased	multivariate adjusted OR	0.97 (0.27, 1.97)		5 or more points using the short form of the Yesavage Geriatric Depression scale was considered indicative of depression; 16% with depression	Age: mean 79.2 (6) years Cognitive impairment: Some patients with cognitive impairment; MMSE; for patients with less than high school education, the cut-off was 21, with HS cut-off was 23, college edu cut-off 24 points); 39% with impaired. Sensory impairment: not stated. Medications: not stated	MV: cognitive impairment, number of MDCs, depression, alcoholism (total scores greater than or equal to 2 using the short form of the Michigan Alcoholism Screening test)	No.events/no. covariates = 85/4 = 21. Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 48/323 (15%) had delirium within 72 hrs of admis; no. pts developing delirium: 85/323 (26.3%) had delirium overall (prevalent + incident)
Rolfson 1999; prospective cohort study in 75 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: moderate	univariate analysis RR	4.5 (0, 0)	p=0.24; CIs not reported;	dichotomous: depression not defined (9% with delirium and 2% without delirium had past depression)	Age: 69-74 years Cognitive impairment: Some patients with cognitive impairment; MMSE less than 24; 9% in group with delirium and 12% in group without delirium. Sensory impairment: not reported. Medications: lorazepam, sufetaniil, midazolam, morphine	MV: past stroke, CPB time (min), low cardiac output	No.events/no. covariates = 23/3 = 8. Number key RFs: 2/4 key RFs: age constant (GDG: narrow age range) and polypharmacy constant. Number of pts with delirium at baseline: None; no. pts developing delirium: 23/71 (32%) patients developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Depression

Outcome measured incidence of delirium

risk factor vs comparator: needs assistance with one or more ADLs vs no assistance

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	0 (0, 0)	No significant; data not reported	dichotomous: depressive symptoms (Geriatric Depression Scal equal to or more than a median score of 80 to 30); 63% in group with delirium and 44% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types

Risk factor: ADL

Outcome measured incidence of delirium

risk factor vs comparator: needs assistance with one or more ADLs vs no assistance

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	0 (0, 0)	Not significant; data not reported	dichotomous: needs assistance with one or more ADLs versus no assistance; 4% in group with delirium and 23% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Infection

Outcome measured ----

risk factor vs comparator: infection vs no infection

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments: risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Levkoff 1988; retrospective cohort study in 1285 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward	multivariate adjusted OR	3.05 (2.02, 4.58)	outcome measured: urinary tract infection	dichotomous: urinary tract infection; 32% in group with delirium and 12% in comparison group Age: not reported Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: sex, emergency or elective admission, age (80+), chronic renal disease, urinary tract infection, sodium, anion gap, creatinine, AST, albumin, calcium, TIBC, haemotocrit, WBC, PT, urine, and proteinuria	Number key RFs: 1/4 key RFs (age). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 117 patients wirh delirium were included in the study and matched wirh 1,168 controls

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Infection

Outcome measured incidence of delirium

risk factor vs comparator: infection vs no infection

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Lin 2008; prospective cohort study in 151 patients. Funding: Unclear/ Not stated. Setting: Hospital; ICU ward . QUALITY RATING: moderate	multivariate adjusted OR	3.65 (1.03, 12.9)		dichotomous: sepsis (defined by the American College of Chest Physicians and the Society of Critical Care Medicine); 80% with sepsis in group with delirium and 57% in group without delirium	Age: 76 years (64-86) Cognitive impairment: Unclear or Not stated; Blessed Dementia Rating Scale of 3 or higher. Patients with dementia excluded.. Sensory impairment: not stated. Medications: Tranquilizers, narcotics, benzodiazepines, steroids	MV: diabetes mellitus, hypoalbuminemia, and sepsis No.events/no. covariates = 31/3 = 10. Number key RFs: 2/4 key RFs (dementia; polypharmacy constant). Number of pts with delirium at baseline: None; no. pts developing delirium: 31/143 (22%) developed delirium
Santos 2004; prospective cohort study in 220 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	6.36 (1.24, 32.7)	p=0.02	dichotomous: postoperative pneumonia; 18/220 (8%)	Age: 66-78 years Cognitive impairment: No patients with cognitive impairment; MMSE (using a cut-off of 23). Sensory impairment: Severe hearing or vision impairment excluded. Medications: Diuretics, calcium channel blockers, beta blockers, ACE inhibitors, nitrates, H2 blockers, diazepam, midozalam	MV: Those included in final model were age, blood urea, cardiothoracic index greater than 0.5, hypertension, smoking, blood replacement (intraoperative), atrial fibrillation, pneumonia, blood balance on 2nd day after surgery Number key RFs: 3-4/4 (age; dementia + sens. imp excluded; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 74/220 (34%) developed delirium after surgery
Schor 1992; prospective cohort study in 291 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	2.96 (1.42, 6.15)		dichotomous: infection versus no infection; 37% with infection in group with delirium and 17% in group without delirium	Age: 80.5 years (SD 7.6) Cognitive impairment: Some patients with cognitive impairment; method not reported; 42% with prior cognitive impairment in the group with delirium and 10% in group without delirium. Sensory impairment: 33% with vision loss and 21% with hearing loss. Medications: Neuroleptics, narcotics, H2 blocker, digoxin, anticholinergics, benzodiazepine, steroids, nonsteroidal anti-inflammatory	MV: age (greater than 80), prior cognitive impairment, fracture on admission, patients from an institution, male sex, infection, pain (poorly controlled), neuroleptic use, and narcotic use Number key RFs: 3/4 key RFs (age, dementia, and possibly sensory impairment). Number of pts with delirium at baseline: Patients with delirium on admission were excluded; no. pts developing delirium: 91/291 (31%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Infection

Outcome measured duration of delirium

risk factor vs comparator: infection vs no infection

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Ely 2007; prospective cohort study in 53 patients. Funding: Mixed. Setting: Hospital; ICU ward (unclear/not stated surgery)	multivariate adjusted OR	1.73 (0.57, 5.3)	p=0.33	dichotomous: sepsis and/or acute respiratory distress syndrome and/or pneumonia; 8/53 (15%) sepsis, 12/53 (23%) pneumonia	Age: 31-79 years Cognitive impairment: Some patients with cognitive impairment; Baseline dementia reported in 16% (7/44) patients; assessment using Questionnaire on Cognitive Decline in the Elderly. Sensory impairment: not stated. Medications: Lorazepam	MV: APOE4 allele (present/absent); age in years, Acute Physiology and Chronic Health Evaluation II score (continuous), coma days (continuous), sepsis/acute respiratory distress syndrome/pneumonia (dichotomous), lorazepam total dose (continuous) Number key RFs: 2/4 (age; polypharmacy constant). Number of pts with delirium at baseline: Not stated; no. pts developing delirium: 47/53 (89%) developed delirium at some point during the ICU stay

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Polypharmacy

Outcome measured incidence of delirium

risk factor vs comparator: >3 medications vs ≤ 3 medications

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Goldenberg 2006; prospective cohort study in 77 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (hip fracture surgery)	multivariate adjusted OR	33.6 (1.9, 591.6)		Use of more than 3 medications (other than vitamins) were considered as use of multiple medications; 67/77 (87%). Psychoactive medications analysed as a separate variable	Age: 81.9 years (66 to 98) Cognitive impairment: Some patients with cognitive impairment; MMSE and Set Test (ST)(poss high score 30 on both); 43 pts-mild dementia MMSE score >16. Mean MMSE= 21.6 (range 2-30); Mean ST score= 20.2 (1-30). Sensory impairment: not stated. Medications: Not stated	MV: multiple medications, low scores on cognitive tests (ST score<20; MMSE score <24), decreased albumin level (<3.5 g/dL), decreased hematocrit level (<33%), age >81 years Number key RFs: 3/4 (not sens. imp). Number of pts with delirium at baseline: None; no. pts developing delirium: 37/77 patients had postoperative delirium

risk factor vs comparator: >7 medications vs <7 medications

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Ranhoff 2006; prospective cohort study in 401 patients. Funding: Grant- other. Setting: Hospital; ICU ward	multivariate adjusted OR	1.9 (1.1, 3.2)		dichotomous: the maximum concurrent number of drugs (all, including laxatives); 7 or more drugs versus less than 7. mean no. of drugs: no delirium group 7.3 (SD 3.1); delirium group 8.2 (SD 3.3)	Age: 60-94 years; 78.1years (SD 8.8) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score two weeks prior to admission to SICU was 19.1 (11.0). Sensory impairment: 116/401 (29%) with vision impairment; patient/close relative asjed if vision problems affecting daily activity. Medications: mean no. of drugs: no delirium group 7.3 (SD 3.1); delirium group 8.2 (SD 3.3)	MV: age, dementia, vision impairment, history of heavy alcohol use, number of drugs taken, s-albumin, APS score, fitted bladder catheter Number key RFs: 4/4. Number of pts with delirium at baseline: 62/401(16%) within 24 hrs of admission; no. pts developing delirium: Cumulative delirium (117/401 (29%); 55/401 (16%) developed delirium during the SICU stay

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: **Sensory impairment**

Outcome measured incidence of delirium

risk factor vs comparator: impaired hearing vs normal hearing

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	0 (0, 0)	Not significant; no data reported	dichotomous: hearing impairment; 78% in group with delirium versus 73% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types

Number key RFs: 3/4 key RFs (not polypharmacy).
Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Sensory impairment

Outcome measured incidence of delirium

risk factor vs comparator: impaired vision vs normal vision

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted HR	4.52 (2.27, 8.98)	HR	Impaired vision; 31% visual impairment, as reported by the patients	Age: 77 years (65-96) Cognitive impairment: No patients with established diagnosis of mental disease or already confused excluded. Sensory impairment: 31% visual and 39% hearing impairment, as reported by the patients. Medications: not stated	MV: marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss; time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time, age, gender...	Number key RFs: 4/4 (patients with dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium:
Ranhoff 2006; prospective cohort study in 401 patients. Funding: Grant- other. Setting: Hospital; ICU ward	multivariate adjusted OR	1.7 (1, 3.1)		visual problems: the patients and/or a close relative were asked if the patient has vision problems affecting daily activity. 116/401 (29%) with vision impairment	Age: 60-94 years; 8.1 years (8.8) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score two weeks prior to admission to SICU was 19.1 (11.0). Sensory impairment: 116/401 (29%) with vision impairment; patient/close relative asked if vision problems affecting daily activity. Medications: not stated	MV: age, dementia, vision impairment, history of heavy alcohol use, number of drugs taken, s-albumin, APS score, fitted bladder catheter	Number key RFs: 4/4. Number of pts with delirium at baseline: 62/401(16%) within 24 hrs of admission; no. pts developing delirium: Cumulative delirium (117/401 (29%); 55/401 (16%) developed delirium during the SICU stay
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward . QUALITY RATING: low	multivariate adjusted RR	3.51 (1.15, 10.71)		vision impairment: corrected vision worse than 20/70 on both near and distant binocular tests; 14% in group with delirium versus 3% in group. Without delirium (data calculated). Standard vision tests (Jaeger and Snellen-type tests).	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% vision impairment; 54% hearing. Jaeger & Snellen tests (vision); Welch-Allyn audioscope; screening questions (hearing).. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types	No.events/no. covariates = 27/13 = 2. Number key RFs: 3/4 key RFs (not polypharmacy). Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: **Severity of illness**

Outcome measured incidence of delirium

risk factor vs comparator: illness severity as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Levkoff 1992 community; prospective cohort study in 211 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	1.1 (1.01, 1.28)		Continuous: sum of severity scores assigned to 15 medical conditions to obtain a score based on the presence and severity of the conditions (range 1-4: unlikely to have impact on care - life threatening); no details given	Age: 78.1years (SD 6.8) Cognitive impairment: Some patients with cognitive impairment; 14% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 8/211 (4%) with delirium at admission; no. pts developing delirium: Community setting (n=211); 43/211 (21%) developed delirium
Levkoff 1992 institution; prospective cohort study in 114 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	0.84 (0.72, 0.98)		Continuous: sum of severity scores assigned to 15 medical conditions to obtain a score based on the presence and severity of the conditions (range 1-4: unlikely to have impact on care - life threatening); no details given	Age: 87.4years (SD7.7) Cognitive impairment: Some patients with cognitive impairment; 42% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 26/114 (23%) with delirium at admission; no. pts developing delirium: Institution (n=114) 48/114 (55%) developed delirium
Quimet 2007; prospective cohort study in 764 patients. Funding: Unclear/ Not stated. Setting: Hospital; ICU ward (unclear/not stated surgery). QUALITY RATING: moderate	multivariate adjusted OR	1.25 (1.03, 1.07)	per-5 point APACHE II increment	Acute Physiology and Chronic Health Evaluation (APACHE) II score 5-point increment; pts with delirium 17.9 (SD 8.2), no delirium 14.0 (8.1)	Age: 48-78 years Cognitive impairment: Unclear or Not stated; Not stated. Sensory impairment: not stated. Medications: Opiates, benzodiazepine, propofol, indomethacin	UV & MV (only significant variables reported): age, hypertension, active tobacco consumption, alcohol consumption, APACHE II score, epidural catheter use, opiate dose, benzodiazepine dose, propofol dose, idomethacin dose, coma, anxiety, pain No.events/no. covariates = 243/13 = 19. Number key RFs: 2/4 (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 243/764(32%) developed delirium in ICU

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: **Severity of illness**

Outcome measured incidence of delirium

risk factor vs comparator: illness severity as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Pisani 2007; prospective cohort study in 304 patients. Funding: Grant- other. Setting: Hospital; ICU ward	multivariate adjusted OR	no data	NS results not reported	continuous: APACHE II score; 24.7 (SD 6.1 delirium, 20.0 (5.6) no delirium)	Age: 66-83 years Cognitive impairment: Some patients with cognitive impairment; baseline dementia assessed using IQCODE. Sensory impairment: 11% with vision impairment and 17% with hearing impairment; proxy reported. Medications: Benzodiazepine, narcotics	MV: nonwhite race, medicaid status, alcohol , history of depression, dementia (score greater than 3.3), APACHE II score (mean) (scale), any impairment of ADL, medication use, admitting diagnosis, admitting physiologic variables, admitting laboratory data. A number of relevant variables were included in the MV, but not presented in the final model = not significant Number key RFs: 2/4 (dementia; polypharmacy constant). Number of pts with delirium at baseline: not clear; no. pts developing delirium: 214/304 (71%) developed delirium within first 48 hrs of ICU admission

risk factor vs comparator: impaired hearing vs normal hearing

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Inouye 1993; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Medical ward	multivariate adjusted RR	3.49 (1.48, 8.23)		dichotomous: severe illness; composite score defined by a nurse rating of severe or an APACHE score or more than 16; 44% in group with delirium and 10% in group without delirium (data calculated)	Age: 79.3 years (SD 6.6) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score 24.2 (5.0); 36% with a score below 24. Sensory impairment: 6% with vision impairment; 54% hearing impairment. Medications: not stated	MV: age, sex, needs assistance with one or more ADLs, needs assistance with two or more ADLs, vision impairment, hearing impairment, MMSE score below 24, history of confusion, illness severity, APACHE score greater than 16, and a composite measure), blood urea nitrogen/creatinine ratio of 18 or more, depressive symptoms, six or fewer social supports, fewer support types Number key RFs: 3/4 key RFs (not polypharmacy). Number of pts with delirium at baseline: None; no. pts developing delirium: 27/107 (25%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: **Severity of illness**

Outcome measured duration of delirium

risk factor vs comparator: APACHE II as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Ely 2007; prospective cohort study in 53 patients. Funding: Mixed. Setting: Hospital; ICU ward (unclear/not stated surgery)	multivariate adjusted OR	0.98 (0.89, 1.06)	p=0.56	continuous: Acute Physiology and Chronic Health Evaluation II score	Age: 31-79 years Cognitive impairment: Some patients with cognitive impairment; Baseline dementia reported in 16% (7/44) patients; assessment using Questionnaire on Cognitive Decline in the Elderly. Sensory impairment: not stated. Medications: Lorazepam	MV: APOE4 allele (present/absent); age in years, Acute Physiology and Chronic Health Evaluation II score (continuous), coma days (continuous), sepsis/acute respiratory distress syndrome/pneumonia (dichotomous), lorazepam total dose (continuous) Number key RFs: 2/4 (age; polypharmacy constant). Number of pts with delirium at baseline: Not stated; no. pts developing delirium: 47/53 (89%) developed delirium at some point during the ICU stay

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Comorbidity

Outcome measured incidence of delirium

risk factor vs comparator: > 4 physical diseases vs < 4 physical diseases

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted HR	15.94 (4.6, 55.31)	HR	dichotomous: 4 or more physical diseases; 10/457 (2%)	Age: 77 years (65-96) Cognitive impairment: No patients with cognitive impairment; patients with established diagnosis of mental disease or already confused excluded. Sensory impairment: 31% visual and 39% hearing impairment. Medications: not stated	MV: marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss; time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time, age, gender... Number key RFs: 4/4 (patients with dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium:

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Comorbidity

Outcome measured incidence of delirium

risk factor vs comparator: illness severity as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Pompei 1994_Chicago; prospective cohort study in 432 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	1.68 (1.37, 2.07)		continuous: number of Major Diagnostic Categories (MDCs) (as a measure of comorbidity); patients with delirium 4.2 (1.6), no delirium 2.9 (1.5)	Age: 68-83 years Cognitive impairment: Some patients with cognitive impairment; MMSE. Sensory impairment: not stated. Medications: not stated	MV: cognitive impairment, number of MDCs, depression, alcoholism (total scores greater than or equal to 2 using the short form of the Michigan Alcoholism Screening test) Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 21/432 (5%) had delirium within 72 hrs of admiss; no. pts developing delirium: 64/432 (15%) had delirium overall (prevalent + incident)
Pompei 1994_Yale; prospective cohort study in 323 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	1.28 (1.02, 1.61)	NO LONGER SIGNIFICANT when incident delirium patients only considered	continuous: number of Major Diagnostic Categories (MDCs) (as a measure of comorbidity); mean 2.9 (SD 1.3)	Age: 79.2years (SD 6) Cognitive impairment: Some patients with cognitive impairment; MMSE; for patients with less than high school education, the cut-off was 21, with HS cut-off was 23, college edu cut-off 24 points); 39% with impaired. Sensory impairment: not stated. Medications: not stated	MV: cognitive impairment, number of MDCs, depression, alcoholism (total scores greater than or equal to 2 using the short form of the Michigan Alcoholism Screening test) Number key RFs: 1/4 (dementia). Number of pts with delirium at baseline: 48/323 (15%) had delirium within 72 hrs of admiss; no. pts developing delirium: 85/323 (26.3%) had delirium overall (prevalent + incident)

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Patient risk factors

Risk factor: Sleep deprivation

Outcome measured incidence of delirium

risk factor vs comparator: sleep deprivation vs no sleep deprivation

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Yildizeli 2005; retrospective cohort study in 432 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (thoracic surgery)	beta from regression (standardised)	1.73 (0, 0)	SE 0.881	2/23 patients with delirium had sleeplessness (8%)	Age: 18-86 years (mean 51.7) Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Aminophylline, antiarrhythmics, antibiotics, steroids, antihypertensives	UV & MV: (preoperative variables) age, sex, chronic disease, alcohol abuse, psychiatric problems, diabetes, cerebrovascular disease, chemotherapy, operation due to malignancy, urgent operation, (postoperative variables) respiratory insufficiency; abnormal serum chemistry values, operation time, LOS, length of ICU stay, sleep deprivation, hypertension, infection, blood transfusion, use of various drugs, immobilisation	Number key RFs: 1/4 RFs (age). Number of pts with delirium at baseline: None; no. pts developing delirium: 23/432 (5%) developed postoperative delirium
Yildizeli 2005; retrospective cohort study in 432 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (thoracic surgery)	multivariate adjusted OR	1.04 (0, 0)	CI's not reported	2/23 patients with delirium had sleeplessness (8%)	Age: 18-86 years (mean 51.7) Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Aminophylline, antiarrhythmics, antibiotics, steroids, antihypertensives	UV & MV: (preoperative variables) age, sex, chronic disease, alcohol abuse, psychiatric problems, diabetes, cerebrovascular disease, chemotherapy, operation due to malignancy, urgent operation, (postoperative variables) respiratory insufficiency; abnormal serum chemistry values, operation time, LOS, length of ICU stay, sleep deprivation, hypertension, infection, blood transfusion, use of various drugs, immobilisation	Number key RFs: 1/4 RFs (age). Number of pts with delirium at baseline: None; no. pts developing delirium: 23/432 (5%) developed postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Environmental risk factors

Risk factor: Institutionalisation

Outcome measured incidence of delirium

risk factor vs comparator: institutionalisation vs community

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Levkoff 1992; prospective cohort study in 325 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	2.16 (1.15, 4.1)		institutional setting pre-hospital versus living in the community; 35% in institution	Age: 81.4 years (SD 7.7) Cognitive impairment: Some patients with cognitive impairment; 24% with preexisting cognitive impairment; assessment methods not reported (relied on medical chart review). Sensory impairment: Patients with severe sensory impairment excluded. Medications: not stated	UV and MV: age, sex, preexisting cognitive impairment (presence/absence), and illness severity	Number key RFs: 3/4 (age, dementia, sensory imp. excl). Number of pts with delirium at baseline: 34/325 (11%) with delirium at admission; no. pts developing delirium: 91/291 (31%) without prevalent delirium developed delirium. Analysis only for incident cases.
Schor 1992; prospective cohort study in 291 patients. Funding: Grant- other. Setting: Hospital; Mixed: Medical/Surgical ward (unclear/not stated surgery)	multivariate adjusted OR	no data	not significant; no data	institutional setting pre-hospital versus living in the community; 30% in institution	Age: 80.5 years (SD 7.6) Cognitive impairment: Some patients with cognitive impairment; method not reported; 42% with prior cognitive impairment in the group with delirium and 10% in group without delirium. Sensory impairment: 33% with vision loss and 21% with hearing loss. Medications: Neuroleptics, narcotics, H2 blocker, digoxin, anticholinergics, benzodiazepine, steroids, nonsteroidal anti-inflammatory	MV: age (greater than 80), prior cognitive impairment, fracture on admission, patients from an institution, male sex, infection, pain (poorly controlled), neuroleptic use, and narcotic use	Number key RFs: 3/4 key RFs (age, dementia, and possibly sensory impairment). Number of pts with delirium at baseline: Patients with delirium on admission were excluded; no. pts developing delirium: 91/291 (31%) developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Environmental risk factors

Risk factor: Institutionalisation

Outcome measured incidence of delirium

risk factor vs comparator: sheltered accommodation vs community

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted OR	no data	not significant; no data	sheltered accommodation versus living in own home; 11% in sheltered accommodation	Age: mean 77 years (65-96 years) Cognitive impairment: No patients with cognitive impairment; patients with mental disease or confused excluded. Sensory impairment: 31% visual and 39% hearing impairment. Medications: not stated	MV: marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss, time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time, age, gender.... Number key RFs: 4/4 (patients with dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium: 51/457 developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Type of surgery

Outcome measured incidence of delirium

risk factor vs comparator: breast and skin surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	0.46 (0.36, 0.59)		categorical: breast and skin surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

risk factor vs comparator: head and neck surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	0.39 (0.3, 0.5)		categorical: head and neck surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Type of surgery

Outcome measured incidence of delirium

risk factor vs comparator: lower urologic and gynaecologic surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	0.55 (0.48, 0.62)		categorical: lower urologic and gynaecologic surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

risk factor vs comparator: musculoskeletal surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.19 (1.08, 1.31)		categorical: musculoskeletal surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Type of surgery

Outcome measured incidence of delirium

risk factor vs comparator: neurological surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.22 (1, 1.49)		categorical: neurological surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

risk factor vs comparator: ophthalmologic surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.2 (1.19, 1.21)		categorical: ophthalmologic surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: **Type of surgery**

Outcome measured incidence of delirium

risk factor vs comparator: thoracic surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.54 (0.95, 1.31)	not significant	categorical: thoracic surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Type of surgery

Outcome measured incidence of delirium

risk factor vs comparator: vascular surgery vs abdominal, retroperitoneal and unclassified surgery

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.2 (1.06, 1.36)		categorical: vascular surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium
Rudolph 2007; prospective cohort study in 1218 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted RR	2.7 (1.7, 4.2)		vascular surgery was compared to all other surgical procedures (abdominal, orthopaedic, genitourinary, thoracic and other)	Age: 68.9 years (SD5.9) Cognitive impairment: Some patients with cognitive impairment; MMSE; mean 27.8 (1.6) at baseline; various other neropsychologic tests applied = mild cognitive impairment. Sensory impairment: not stated. Medications: not stated	MV: age, male, any tobacco exposure, diabetes, previous myocardial infarction, vascular surgery	Number key RFs: 2/4 (age; dementia constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: cumulative incidence was 99/1161 (9%) in the 7-day postoperative period

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Cardiac surgery

Outcome measured incidence of delirium

risk factor vs comparator: Beating heart surgery vs Bypass surgery

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Bucerius 2004; prospective cohort study in 16184 patients. Funding: Unclear/ Not stated. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: moderate	multivariate adjusted OR	0.47 (0.32, 0.69)		Beating heart surgery (no cardiopulmonary bypass) versus bypass (conventional) surgery; 1842/16184 (11%) BH	Age: not stated Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: not stated	MV: Cerebrovascular disease; atrial fibrillation; diabetes; peripheral vascular disease; left ventricular ejection fraction 30% or less; shock; urgent operation; operating time over 3 hours; haemofiltration; transfusion above 2L; beating heart surgery; age (35 variables in total - all not reported) No.events/no. covariates = 1354/35 = 39. Number key RFs: 3/4 (age; dementia and polypharmacy constant). Number of pts with delirium at baseline: Probably no delirium; no. pts developing delirium: 1354/16184 developed postoperative delirium

risk factor vs comparator: CABG-valve surgery vs CABG

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Veliz-Reissmuller 2007; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery). QUALITY RATING: low	multivariate adjusted OR	3.25 (0.8, 13)	CABG-valve versus CABG	Coronary artery bypass grafting (CABG)-valve sugery versus CABG	Age: 65-78 years Cognitive impairment: Some patients with cognitive impairment; MMSE; the median score was 29 (17-30) in the delirium group and 30 (27-30) in the non-delirium group. Sensory impairment: not stated. Medications: not stated	MV: age, alcohol consumption, memory complaints, CABG- valve versus CABG, valve versus CABG, preoperative MMSE score (less than or equal to 28 versus greater than or equal to 29 points) No.events/no. covariates = 25/6 = 4. Number key RFs: 3/4 (age and cognitive impairment; polypharmacy constant). Number of pts with delirium at baseline: not clear (not recorded preop); no. pts developing delirium: 25/107 (23%) developed delirium postoperatively

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Cardiac surgery

Outcome measured incidence of delirium

risk factor vs comparator: cardiac surgery vs abdominal, retroperitoneal and unclassified surgery

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.12 (0.95, 1.31)	p=0.18	categorical: cardiac surgery versus abdominal, retroperitoneal or unclassified surgery	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

risk factor vs comparator: CPB time as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Rolfson 1999; prospective cohort study in 75 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	1.02 (1, 1.04)	p=0.05	continuous: CPB time (mins) (mean time was 83 mins in the group with delirium and 58 mins in the group without delirium)	Age: 69-74 years Cognitive impairment: Some patients with cognitive impairment; MMSE less than 24; 9% in group with delirium and 12% in group without delirium. Sensory impairment: not reported. Medications: lorazepam, sufentanil, midazolam, morphine	MV: past stroke, CPB time (min), low cardiac output	Number key RFs: 2/4 (age and polypharmacy constant). Number of pts with delirium at baseline: None; no. pts developing delirium: 23/71 (32%) patients developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Cardiac surgery

Outcome measured incidence of delirium

risk factor vs comparator: valve surgery vs CABG

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Veliz-Reissmuller 2007; prospective cohort study in 107 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (cardiac surgery)	multivariate adjusted OR	3.9 (1, 15.8)	valve versus CABG	valve surgery versus CABG	Age: 65-78 years Cognitive impairment: Some patients with cognitive impairment; MMSE; the median score was 29 (17-30) in the delirium group and 30 (27-30) in the non-delirium group. Sensory impairment: not stated. Medications: not stated	MV: age, alcohol consumption, memory complaints, CABG- valve versus CABG, valve versus CABG, preoperative MMSE score (less than or equal to 28 versus greater than or equal to 29 points) Number key RFs: 3/4 (age and cognitive impairment; polypharmacy constant). Number of pts with delirium at baseline: not clear (not recorded preop); no. pts developing delirium: 25/107 (23%) developed delirium postoperatively

Risk factor: Emergency surgery

Outcome measured incidence of delirium

risk factor vs comparator: emergency surgery vs elective surgery

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery). QUALITY RATING: low	multivariate adjusted HR	4.74 (1.76, 12.8)	outcome reported was hazard ratio (exp (B))	emergency admission for hip fracture versus elective surgery for coxarthros or gonarthros; 208/457 (46%) emergency	Age: 77 years (65-96) Cognitive impairment: No patients with cognitive impairment; patients with mental disease or confused excluded. Sensory impairment: 31% visual and 39% hearing impairment. Medications: not stated	MV: marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss, time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time, age, gender No.events/no. covariates = 51/24 = 2. Number key RFs: 4/4 (patients with dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium: 51/457 developed delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: duration of surgery

Outcome measured incidence of delirium

risk factor vs comparator: duration of surgery as continuous variable

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>	
Redelmeier 2008; retrospective cohort study in 284158 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (likely to be mixed surgery)	multivariate adjusted OR	1.2 30 min (1.19, 1.21)		continuous: duration of surgery, per 30-minute increase	Age: 67-80 years Cognitive impairment: Unclear or Not stated; not stated. Sensory impairment: not stated. Medications: Statins, non-statin lipid lowering medications, antihypertensives, diuretics, misc. cardiovascular agents, antiplatelet agents, orally administered anticoagulants, other vascular agents, and others	MV: age, sex, neuropsychiatric drug (4 different drugs), type of surgery (cardiac, thoracic, neurosurgical, vascular, musculoskeletal, lower urologic and gynecologic, breast and skin, external head and neck, ophthalmologic), duration of surgery (per 30-min increase)	Number key RFs: 2 key RFs (age; polypharmacy constant). Number of pts with delirium at baseline: Not clear; no. pts developing delirium: 3195/284158 (1%) had postoperative delirium

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Iatrogenic intervention

Outcome measured incidence of delirium

risk factor vs comparator: bladder catheter vs no bladder catheter

Study name	Outcome	Sum stats (95%CI)	comments:	risk factor details:	other details:	factors adjusted for in multivariate analysis
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted HR	0 (0, 0)	Not significant; no data reported	dichotomous: catheter in the bladder (no details provided)	Age: 77 years (65-96) Cognitive impairment: No patients with cognitive impairment; patients with established diagnosis of mental disease or already confused excluded. Sensory impairment: 31% visual and 39% hearing impairment. Medications: not stated	MV: marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss; time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time, age, gender...
Ranhoff 2006; prospective cohort study in 401 patients. Funding: Grant- other. Setting: Hospital; ICU ward	multivariate adjusted OR	2.7 (1.4, 4.9)		Fitted bladder catheter; 228/401 (57%)	Age: 60-94 years; 78.1 years (8.8) years Cognitive impairment: Some patients with cognitive impairment; MMSE; mean score two weeks prior to admission to SICU was 19.1 (11.0). Sensory impairment: 116/401 (29%) with vision impairment; patient/close relative asjed if vision problems affecting daily activity. Medications: not stated	MV: age, dementia, vision impairment, history of heavy alcohol use, number of drugs taken, s-albumin, APS score, fitted bladder catheter

Number key RFs: 4/4 (patients with dementia excluded).
Number of pts with delirium at baseline: None; no. pts developing delirium:

Number key RFs: 4/4.
Number of pts with delirium at baseline: 62/401(16%) within 24 hrs of admission; no. pts developing delirium: Cumulative delirium (117/401 (29%); 55/401 (16%) developed delirium during the SICU stay

Appendix F: Multivariate risk factors: Non pharmacological risk factors

Procedural risk factors

Risk factor: Iatrogenic intervention

Outcome measured incidence of delirium

risk factor vs comparator: preoperative medical treatment vs no preop treatment

<i>Study name</i>	<i>Outcome</i>	<i>Sum stats (95%CI)</i>	<i>comments:</i>	<i>risk factor details:</i>	<i>other details:</i>	<i>factors adjusted for in multivariate analysis</i>
Andersson 2001; prospective cohort study in 457 patients. Funding: Grant- other. Setting: Hospital; Surgical ward (fracture neck of femur surgery)	multivariate adjusted HR	2.66 (1.26, 5.62)	HR	preoperative medical treatment (yes or no) 37/457 (8%)	Age: 77 years (65-96) Cognitive impairment: No patients with cognitive impairment; patients with established diagnosis of mental disease or already confused excluded. Sensory impairment: 31% visual and 39% hearing impairment. Medications: not stated	MV: marital status, cohabitation, housing, need for help before admission, mobility, hearing, vision, reason for admission, number of other diseases, postoperative complications, preoperative medication, method and length of anaesthesia, blood loss; time admission to surgery, OBS score on admission, type of fracture, antibiotics, catheter, traction, hour of admission, surgery time, age, gender... Number key RFs: 4/4 (patients with dementia excluded). Number of pts with delirium at baseline: None; no. pts developing delirium: 51/457 developed delirium