Appendix E: Cohort studies - methodological quality: Non pharmacological risk factors

Study	Delirium Assessment	Representa tiveness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Andersson 2001; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: ratio of events/covariate 2 or 3	51/24 (=2)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up; All patients followed up until discharge	Not stated/ unclear	Prospective cohort but inadequate numbers of patients for number of variables studied; 4/4 key RFs: patients with dementia excluded

Evidence quality: low

Bohner 2003; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible: not enough patients for multivariate analysis	60/9 (=7)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up; follow up for 7 days	Not stated/ unclear	prospective cohort but not enough events per variable; 3/4 key RFs (age; dementia and polypharmacy constant because cardiac surgery patients)

Evidence quality: moderate

Bucerius 2004; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Fairly acceptable: nearly enough key risk factors	1354/35 (=39)	Exposed/non-exposed from same cohort	Unclear	Adequate: all patients followed up; data complete for each patient	Not stated/ unclear	Large prospective cohort; 3/4 key RFs: age; dementia and polypharmacy constant because cardiac bypass surgery patients; unclear if prevalent delirium

Evidence quality: moderate

Caeiro 2004; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: only 1/4 key risk factors	29/4 (=7)	Exposed/non-exposed from same cohort	Unclear	Acceptable: ≤20% loss to follow up; 220 at start; 2 assessment not completed	Not stated/ unclear	Prospective cohort; acute stroke; not enough events per variable; only 1/4 key RFs (age); general medical. Unstated how cognitive impairment assessed.

Evidence quality: low

Edlund 2001; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounded: no key risk factors	19/8 (=2)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Acceptable: ≤20% loss to follow up; 2/101 patients did not have full data	Not stated/ unclear	preoperative analysis (61% patients - prevalent delirium) is essentially a cross sectional study; 2/4 key RFs (polypharmacy, dementia). Postop study (incident delirium) had NO KEY RFs

Evidence quality: biased

Ely 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible : not enough factors included	47/6 (=8)	Exposed/non-exposed from same cohort	Patients were in ICU and were likely to have incident delirium	Adequate: all patients followed up; Of 59 patients enrolled, 6 were excluded (coma/death)	Not stated/ unclear	Select group: mechanically ventilated intensive care patients; ratio of events/covariate is 8; 2/4 key RFs (age; polypharmacy constant because ICU)

Evidence quality: moderate

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Furlaneto 2006; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: only 1/4 key risk factors	30/2 (=15)	Exposed/non-exposed from same cohort	Significant, more than half of delirium was prevalent delirium	Adequate: all patients followed up; 7 deaths; 4 in the delirium group and 3 in the control group	Not stated/ unclear	Selected group: elderly patients admitted to geriatric orthopaedic ward; all patients with delirium appear to have been included in the analyses (prevalence 17% and incidence 13%); only 1/4 key RFs: dementia

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Goldenberg 2006; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible: not enough patients for multivariate analysis	37/6 (=6)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	Hip fracture surgery. Not enough events/covariate; 3/4 key RFs (age, dementia, polypharmacy)

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Hofste 1997; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible : not enough factors included	44/5 (=9)	Exposed/non-exposed from same cohort	Unclear	Adequate: all patients followed up;	Not stated/ unclear	Selected group: cardiac surgery patients; 2/4 key RFs: age included; dementia constant because elective cardiac surgery patients; (GDG: blindness/deafness not considered sensory impairment)

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Inouye 1993; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding probable: ratio of events/covariate 2 or 3	27/13 (=2)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	3/4 key RFs: age and sensory impairment included; dementia excluded from analysis

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Inouye 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding possible : not enough factors included	48/5 (=10)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up; No missing data (all analysed)	No	2/4 key RF's taken into account: dementia; vision impairment.

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Kazmierski 2006; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: ratio of events/covariate 2 or 3	30/16 (=2)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	Only cardiac surgery patients included in study; of 296 consecutively admitted patients, 260 were enrolled; ratio 2 events/covariate; 2/4 key RFs : age and cognitive impairment included in analysis

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Korevaar 2005; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding possible: not enough factors included	36/10 (=4)	Exposed/non-exposed from same cohort	Unclear	Adequate: all patients followed up; Of 488 eligible patients,182 were excluded. Of 306, a random sample of 126 patients were selected	Not stated/ unclear	2/4 key RFs (age and cognitive impairment) and ratio of 4 events/covariate; unclear if incident delirium
Leung 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding probable: ratio of events/covariate 2 or 3	29/10 (=3)	Exposed/non-exposed from same cohort	Unclear	Acceptable: ≤20% loss to follow up; 13/203 (6%) lost to follow-up; delirium assessment was not performed on these patients	Not stated/ unclear	2/4 key RF (age, dementia) included in MV analysis; number of events/covariate is 3; unclear initial exposure
Levkoff 1988; Retrospective study	inadequate (e.g.retrospective chart review)	somewhat representative of the community	Confounding probable: only 1/4 key risk factors	117/18 (=6)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	No	Groups were matched according to admitting service: medical, cardiology, neurology, medical oncology, orthopaedics, pychiatry, general surgery, etc.. 1/4 key RFs (age); retrospective; inadequate method of assessment
Levkoff 1992; Prospective study	partly adequate (e.g.MMSE)	somewhat representative of the community	Confounding possible: not enough factors included	91/4 (=23)	Exposed/non-exposed from same cohort	Some patients had prevalent delirium but excluded from analysis	Adequate: all patients followed up; Patients with prevalent delirium (11%) excluded from analysis	Not stated/ unclear	Analysis only for incident delirium; 2-3/4 key RFs: age, dementia; patients with severe sensory impairment were excluded. Delirium assessment based on DSM III. Unstated scale for cognitive impairment.
Levkoff 1992 community; Prospective study	partly adequate (e.g.MMSE)	somewhat representative of the community	Confounding possible: not enough factors included	43/4 (=11)	Exposed/non-exposed from same cohort	Some patients had prevalent delirium but excluded from analysis	Adequate: all patients followed up; Patients with prevalent delirium excluded (4%)	Not stated/ unclear	Overall participation rate 79.5% of eligible patients; results may not be generalisable to all elderly people living in the community; 2-3/4 key RFs (age, dementia + sensory imp. Excl). Unstated how cognitive impairment assessed. DSM III for delirium
Levkoff 1992 institution; Prospective study	partly adequate (e.g.MMSE)	somewhat representative of the community	Confounding possible: not enough factors included	48/4 (=12)	Exposed/non-exposed from same cohort	Some patients had prevalent delirium but excluded from analysis	Adequate: all patients followed up; Patients with prevalent delirium excluded from the analysis (23%)	Not stated/ unclear	Overall participation rate 79.5% of eligible patients; results may not be generalisable to all elderly people living in institutions; 3/4 key RFs (age, dementia + severe sensory imp. Excl). Unstated how cognitive impairment assessed. DSM III for delirium

Evidence quality: low

Evidence quality: low

Evidence quality: biased

Evidence quality: moderate

Evidence quality: moderate

Evidence quality: moderate

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Lin 2008; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible : not enough factors included	31/3 (=10)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Acceptable: ≤20% loss to follow up; 8/151 (5%) remained comotose throughout the investigation	No	Selected group: mechanically ventillated patients; 1-2/4 key RFs: dementia excluded and polypharmacy held constant because ICU patients

Evidence quality: moderate

McCusker 2001; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Fairly acceptable: nearly enough key risk factors	444/24 (=18)	Exposed/non-exposed from same cohort	Some patients had delirium at start of study	Not stated;	Not stated/ unclear	Repeated measures analyses (patients included >1 in different states). patients with delirium in RCT and 'controls' selected from patients screened for delirium without delirium. Severity using DI tool based on CAM. 3 key RFs.

Evidence quality: low

Ouimet 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible : not enough factors included	243/13 (=19)	Exposed/non-exposed from same cohort	Patients were in ICU and were likely to have incident delirium	Adequate: all patients followed up;	Not stated/ unclear	Only 2/4 key RFs : age; polypharmacy constant because ICU

Evidence quality: moderate

Pisani 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible : not enough factors included	214/24 (=9)	Exposed/non-exposed from same cohort	Patients were in ICU and were likely to have incident delirium	Adequate: all patients followed up;	Not stated/ unclear	Medical/surgical ICU; Of 318 eligible patients, 309 (97%) were enrolled - 5 of which were excluded (coma); ratio of events/covariate is 9; 2/4 key RFs (dementia; polypharmacy constant because ICU)

Evidence quality: moderate

Pompei 1994_Chicago; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding probable: only 1/4 key risk factors	64/4 (=16)	Exposed/non-exposed from same cohort	Some patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	Chicago: Results include 33% prevalent cases; only 1/4 key RFs: dementia. When incident delirium only: dementia and alcoholism no longer significant.

Evidence quality: low

Pompei 1994_Yale; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding probable: only 1/4 key risk factors	85/4 (=21)	Exposed/non-exposed from same cohort	Some patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	Results include 57% prevalent cases overall; only 1/4 key RFs (dementia)

Evidence quality: biased

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Ranhoff 2006; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible: not enough patients for multivariate analysis	55/8 (=7)	Exposed/non-exposed from same cohort	Patients were in ICU and were likely to have incident delirium	Adequate: all patients followed up;	Not stated/ unclear	Selected group: elderly patients in SICU; ratio of events/covariate was 7; 4/4 key RFs (age, dementia, polypharmacy, visual impairment). Prevalent + incident delirium reported; incident was 47%

Evidence quality: moderate

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Redelmeier 2008; Retrospective study	inadequate (e.g.retrospective chart review)	somewhat representative of the community	Confounding possible : not enough factors included	3195/16 (=200)	Exposed/non-exposed from same cohort	Unclear	Adequate: all patients followed up;	No	2/4 key RF's taken into account: age; possibly polypharmacy constant because surgical patients; retrospective; inadequate measurement of delirium

Evidence quality: biased

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Rolfson 1999; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible : not enough factors included	23/3 (=8)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Acceptable: ≤20% loss to follow up; 4/75 (5%) lost to follow-up (3 died and 1 was comotose at follow-up)	Yes (and number not met)	Some variables not comparable (evaluated in UV analysis). elderly patients undergoing CABG surgery; assuming alpha=0.05, beta=0.20, and a desired margin of error of 0.10, with 30% delirium, a sample size of 81 was estimated; 2/4 key RFs: age constant (GDG: narrow age range) and polypharmacy constant

Evidence quality: moderate

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Rudolph 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	somewhat representative of the community	Confounding possible : not enough factors included	99/6 (=16)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Acceptable: ≤20% loss to follow up; 57/1218 (5%) did not have postoperative delirium assessments	Not stated/ unclear	Only 1-2/4 key RFs (age included in MV analysis; dementia excluded (held constant), but mild cognitive impairment patients included). Appears to include prevalent cases (no details).

Evidence quality: moderate

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Santos 2004; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: ratio of events/covariate 2 or 3	74/36 (=2)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	Elderly cardiac surgery patients chosen randomly by drawing lots; ratio events/covariate was 2; 3-4/4 key RFs (age; dementia + severe sens. imp excluded, polypharmacy constant because cardiac surgery patients)

Evidence quality: low

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Schor 1992; Prospective study	partly adequate (e.g.MMSE)	somewhat representative of the community	Confounding possible : not enough factors included	91/9 (=10)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	No	2-3/4 key RF's taken into account: age dementia; patients wih severe hearing or vision loss excluded from study. Delirium assessment using DSI (based on DSM III). Unstated how cognitive impairment assessed.

Evidence quality: moderate

Study	Delirium Assessment	Representativeness	Cohort comparability	pts per covariate	source of population	Initial exposure	Loss to follow up	Sample size	Overall Comments
Sheng 2006; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: ratio of events/covariate 2 or 3	39/14 (=3)	Exposed/non-exposed from same cohort	Unclear	Adequate: all patients followed up; All patients followed up for risk factor analysis	Not stated/ unclear	Select group: acute stroke patients; not enough patients for MV analysis; 3/4 key RFs (age, dementia, sensory impairment)

Evidence quality: low

Veliz-Reissmuller 2007; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding possible: not enough patients for multivariate analysis	25/6 (=4)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Acceptable: ≤20% loss to follow up; 3/107 (3%) patients died and were no cognitively assessed at discharge	Not stated/ unclear	Select group: elective cardiac surgery; ratio of events/covariate is 4 and 3/4 key RFs: age and cognitive impairment, polypharmacy constant because cardiac operations. Inappropriate cut off on MMSE for cognitive impairment

Evidence quality: low

Yildizeli 2005; Retrospective study	inadequate (e.g.retrospective chart review)	selected group eg specific operations	Confounded: ratio of events/covariate less than 1	23/25 (=1)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up; 3 patients died but data analysed	Not stated/ unclear	Selected group: thoracic surgery patients; not enough patients for MV analysis; retrospective; 1/4 key RFs: age

Evidence quality: biased

Zakriya 2002; Prospective study	adequate (e.g. CAM/DSM IV validated)	selected group eg specific operations	Confounding probable: only 1/4 key risk factors	47/6 (=8)	Exposed/non-exposed from same cohort	No patients had delirium at start of study	Adequate: all patients followed up;	Not stated/ unclear	Select group: elderly hip fracture patients; nearly enough patients in MV analysis; only 0-1/4 key RFs: dementia excluded (not stated how measured)

Evidence quality: low