		Strength of	Quality of	References	
	mmendation Statement	Recommendation	Evidence		
Stror	ng Recommendations	Γ	•	1	
Π.	Healthcare systems and hospitals should implement multicomponent nonpharmacologic intervention programs delivered by an interdisciplinary team (including physicians, nurses, and possibly other healthcare professionals) for the entire hospitalization in at-risk older adults undergoing surgery to prevent delirium.	Strong	Moderate	Inouye 1999 Inouye 2000 Holt 2013 Martinez 2012 Rubin 2006 Bjorkelund 2010 Vidan 2009 Inouye 2000 Lundstrom 2007 Chen 2011 Inouye 2003	
Ι.	Healthcare systems and hospitals should implement formal educational programs with ongoing formal and/or informal refresher sessions for healthcare professionals on delirium in at-risk older surgical adults to improve understanding of its epidemiology, assessment, prevention, and treatment.	Strong	Low	Lundstrom 2005 Tabat 2005 Robinson 2008	
IV.	The healthcare professional should perform a medical evaluation, make medication and/or environmental adjustments, and order appropriate diagnostic tests and clinical consultations after an older adult has been diagnosed with postoperative delirium to identify and manage underlying contributors to delirium.	Strong	Low	Heymann 2010 Milisen 2001 Pitkala 2006 Mudge 2013 Young 2003	
VIII.	Healthcare professionals should optimize postoperative pain control, preferably with nonopioid pain medications, to minimize pain in older adults to prevent delirium.	Strong	Low	Vaurio 2006 Lynch 1998 Leung 2006 Krenk 2012	
IX.	The prescribing practitioner should avoid medications that induce delirium postoperatively in older adults to prevent delirium.	Strong	Low	Agostini 2001 Marcantonio 1994 Taipale 2012 Luukkanen 2011	
XI.	In older adults not currently taking cholinesterase inhibitors, the prescribing practitioner should not newly	Strong	Low	Gamberini 2009 Liptzin 2005	

	prescribe cholinesterase inhibitors perioperatively to older adults to prevent or treat delirium.			Marcantonio 2011 Sampson 2007 Overshott 2010 Van Eijk 2010
XIII.	The prescribing practitioner <u>should not</u> use benzodiazepines as a first line treatment of the agitated post-operative delirious patient who is threatening substantial harm to self and/or others <u>to treat</u> <u>postoperative delirium</u> <i>except</i> when benzodiazepines are specifically indicated (including but not limited to treatment of alcohol or benzodiazepine withdrawal). Treatment with benzodiazepines should be at the lowest effective dose for the shortest possible duration, and should be employed only if behavioral measures have failed or are not possible and ongoing use should be evaluated daily with in-person examination of the patient.	Strong	Low	Breitbart 1996 Marcantonio 1994 Pisani 2009 Pandharipande 2006
XIV.	The prescribing practitioner <u>should not</u> prescribe antipsychotic or benzodiazepine medications for the treatment of older adults with postoperative delirium who are not agitated and threatening substantial harm to self or others.	Strong	Low	Hakim 2012 Girard 2010 Breitbart 1996
Weal	Recommendations	L		
111.	Healthcare professionals should consider multicomponent interventions implemented by an interdisciplinary team in older adults diagnosed with postoperative delirium to improve clinical outcomes.	Weak	Low	Lundstrom 2005 Zaubler 2013 Rubin 2006 Inouye 2000 Lundstrom 2007 Milisen 2001 Rubin 2011 Cole 1994 Cole 2002 Mador 2004 Marcantonio 2010 Pitkala 2006 Schweikert 2009
VII.	A healthcare professional trained in regional anesthetic injection may consider providing regional anesthetic at	Weak	Low	Mouzopoulos 2009 Kinjo 2012

	the time of surgery and postoperatively to improve pain control and prevent delirium in older adults.			
XII.	The prescribing practitioner may use antipsychotics at the lowest effective dose for the shortest possible duration to treat patients who are severely agitated or distressed, and are threatening substantial harm to self and/or others. In all cases, treatment with antipsychotics should be employed only if behavioral interventions have failed or are not possible, and ongoing use should be evaluated daily with in-person examination of patients.	Weak	Low	Hakim 2012 Girard 2010 Devlin 2010 Tahir 2010 Maneeton 2013 Han 2004 Grover 2011 Kim 2010 Skrobik 2004 Yoon 2013 Breitbart 1996
Reco	mmendations Without Sufficient Evidence		•	
VI.	The anesthesia practitioner may use processed electroencephalographic (EEG) monitors of anesthetic depth during intravenous sedation or general anesthesia of older patients to reduce postoperative delirium.	Insufficient	Low	Sieber 2010 Santarpino 2011 Chan 2013 Radtke 2013
Х.	There is insufficient evidence to recommend for or against the use of antipsychotic medications prophylactically in older surgical patients to prevent delirium.	Not Applicable	Low	Larsen 2010 Van den Boogaard 2013 Prakanrattana 2007 Wang 2012 Kaneko 1999 Page 2013 Vochteloo 2011 Kalisvaart 2005
V.	There is insufficient evidence to recommend for or against hospitals creating, and healthcare professionals using, specialized hospital units for the inpatient care of older adults with postoperative delirium to improve clinical outcomes.	Not Applicable	Low	Bee Gek Tay 2013 Eeles 2013 Flaherty 2010 Lu 2011 Goldberg 2013

G3-G5-Inouye SK, Bogardus ST, Jr., Charpentier PA, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1999;340(9):669-76.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
nouye 1999	N = 2434 potentially	n = 426 intervention	Delirium assessment:	- MMSE, CAM evaluated daily by	Cost of intervention
JSA	eligible	II - 420 IIItel vention	MMSE	research nurses and experienced	Total = $$139,506$
15A	n = 1169 eligible	Men and women (61%)	CAM		
			CAM	clinical researchers; Hospital day	\$327 per patient in
Setting	n=250 patient, family or	Mean age 79.6 (6.1)	<b>B H H H H H</b>	5 or at discharge (if before day 5)	intervention group
Seneral medicine	physician refused	MMSE = 23.7 (4.6)	Delirium severity (additive	patients reassessed for risk	The cost of intervention per
ervice at a teaching	enrollment	MMSE <24 = 41%	score of 4)	factors of delirium; Delirium	case of delirium prevented
lospital	n=67 matching patient not	Risk of delirium intermediate = 72%	-symptom fluctuation	severity assessed by sum of	was \$6,341 (\$139,506 for 22
	found	Risk of delirium high = 28%	-inattention	scores = delirium severity	cases prevented [64 cases of
Study Design			-disorganized thinking	no significant differences between	delirium occurred in patients
Controlled clinical trial	N=852 final study sample	Protocol	-altered level of	groups	receiving usual care, as
ising prospective	n=426 pairs of patients	1) Elder Life Program was implemented	consciousness		compared with 42 cases in
ndividual matching	receiving study	by a trained interdisciplinary team,			those receiving the
Ũ	intervention and usual care	which consisted of	Baseline characteristics	No significant difference between	intervention]).
election method	(see matching procedures	-a geriatric nurse-specialist,		groups	Comments
Consecutive patients	in Comments column)	-two specially trained Elder Life		Of all baseline assessments, only	Intervention was most
dmitted to the		specialists.		MMSE <24 was associated with	effective in patients who we
eneral-medicine	Inclusion	-a certified therapeutic-recreation		outcome p<0.01	at intermediate risk for
ervice at urban	Age≥70	specialist,			delirium at base line.
eaching hospital	-no delirium at admission	-a physical- therapy consultant,	Primary outcomes	intervention vs. usual-care	definition at base line.
eaching nospital	-intermediate or high risk	-a geriatrician,	Delirium	9.9% vs. 15% p = 0.02	Once an initial episode of
tudy Longth/Ctort	for delirium at base line	5	Secondary outcomes	9.9% vs. 15% p = 0.02	delirium had occurred,
Study Length/Start-	for delinium at base line	-trained volunteers.			
top Dates	<b>_</b>	2) Six risk factors for delirium were	Total number of days of	405 1 404 1 0.00	however, the intervention h
/1995 — 3/1998	Exclusion	targeted for intervention:	delirium	105 days vs. 161 days p = 0.02	no significant effect on the
	N = 1265	-cognitive impairment,	No. episodes of delirium	62. vs. 90 p = 0.03	severity of delirium or on th
Purpose	-inability to participate in	-sleep deprivation,	Overall rate of adherence	87% (8716 of 10,056 patient-	likelihood of recurrence. Th
o compare the	interview	- immobility,		days)	finding has an important
effectiveness of a	n= 154 profound dementia	-visual impairment,	Cognitive impairment improved		implication for the treatmen
nulticomponent	that precluded verbal	<ul> <li>hearing impairment,</li> </ul>	by 2 points	51(40%) vs. 33(26%) p = 0.04	delirium: primary preventior
trategy for reducing	communication	-dehydration	Adjusted orientation score at		probably the most effective
he risk of delirium	n=92 language barrier	<ol><li>adherence to intervention recorded</li></ol>	reassessment	7.2(0.2) vs. 6.8(0.2) p=0.06	strategy
vith that of a usual	n=38 profound aphasia	daily	Use of sedative drug for sleep		
lan of care for	n=14 intubation or	-	during hospital stay	148 (35%) vs. 195 (46%) p=0.001	Matching procedures
ospitalized older	respiratory isolation		Total number of risk factors,		-computerized algorithm
atients, to determine	n-69 coma or terminal		improved (fewer risk factors)	272 (64%) vs 236(55%) p=0.02	designed to match patients
he level of adherence	illness		Adjusted no. risk factors per	(=,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	according to
o the intervention	n=219 hospital stay 48h or		patient at reassessment	1.7(0.1) vs. 1.9(0.1) p=0.001	-age within five years,
protocol, and to	less		patient at reassessment		-sex.
neasure the effect of	n=324 prior enrollment in	n = 426 usual care	Delirium assessment:	See above	-base-line risk of delirium
he intervention on the	this study	n – 420 usual cale	Demium assessment.	See above	(intermediate or high)
argeted risk factors.	n=355 other reasons like	Man and woman (610/)	Peopline characteristics	See above	Predictive model (4 risk
argeleu fisk factors.	II-355 Utilel Teasons like	Men and women (61%)	Baseline characteristics	See above	•
	Evolution wetten to did not	Mean age 79.8 (6.2)	Deles and a second	O a a shava	factors)
Funding source(s):	Excluded patients did not	MMSE 23.3 (4.9)	Primary outcomes	See above	- visual impairment,
Grants from NIA,	differ significantly from the	MMSE <24 45%			-severe illness,
Commonwealth Fund,	852 patients who were	Risk of delirium intermediate 72%	Secondary outcomes	See above	-cognitive impairment,
Retirement Research	enrolled in terms of age,	Risk of delirium high 28%			-high ratio of blood urea
oundation,	sex, or base-line risk of	Protocol			nitrogen to creatinine.
Community	delirium	-standard hospital services provided by			Intermediate risk
oundation for	-larger proportion of	physicians, nurses, and support staff in			-presence of 1 or2 risk
Greater New Haven	patients receiving usual	other general-medicine units.			factors at base line,
	care were excluded (63	-members of the intervention team did			High risk
Quality Score:	percent, vs. 50 percent in	not provide services			-presence of 3 or4 risk
	the intervention group;	- same attending and resident			factors at base line
Risk of Bias:	P=0.001	physicians provided care to patients in			
Inclear		both study groups			
noicai		both study groups			l

no significant effect on the severity of delirium or on recurrence rates; this finding suggests that primary prevention of delirium is probably the most effective treatment strategy.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	1	Low	
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Possible contamination, intervention protocols disseminated by word of mouth to usual care unit staff. Physicians carried over some intervention protocols to usual-care group
OVERALL RISK OF RIAS (Low Linclose, High) broad on 4.6 shows			BIAS RATING = Unclear
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above           7. Validated delirium measure used (indicate which measure) (1 point if used):	1		DIAS RATING - Unclear
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

# G3-G5-Inouye SK. Prevention of delirium in hospitalized older patients: risk factors and targeted intervention strategies. Ann Med. 2000a;32(4):257-63.

Study Characteristics	Population	Studies	Measure	Outcome	Other information
Inouye 2000a USA Setting General medicine service at a university hospital	Delirium Prevention Trial N = 852 enrolled n=426 matched pairs of intervention-control patients	To identify predisposing factors for developing of delirium during hospitalization n = 107 patients first cohort n = 174 second cohort (validated first cohort findings)	>30 potential risk factor variables studied <b>Predisposing risk factors</b> Vision impairments (acuity <20/70) Severe illness (APACHE II >16) Cognitive impairment (MMSE <24) Debydration (PLIN/CP ratio > 19/	RR 3.5 (1.2 – 10.7) RR 3.5 (1.5 – 8.2) RR 2.8 (1.2 – 6.7) RR 2.0 (0.9 – 4.6)	Patients placed in low (no factors present), intermediate (one or tw factors present), or high (three or four factors present) risk groups showed a statistically significant trend towards increasing risk of delivium with increasing numbers
Study Design -prospective studies to examine predisposing and precipitating factors for delirium, -controlled clinical trial intervention using	Inclusion Age ≥ 70 -no evidence of delirium at admission -intermediate to high risk for delirium at baseline	Inclusion Age ≥ 70 -admitted to general medicine service at a university hospital	Dehydration (BUN/CR ratio ≥ 18(		delirium with increasing numbers of predisposing factors. RR for delirium increased from 1.0 in low risk group to 9.2 in high-risk group. -predictive model and risk stratification system validated in the second cohort of patients
prospective individual matching Selection method Delirium Prevention Trial: consecutive patients admitted to general medicine service at	Exclusion Not discussed ****** Delirium Prevention Trial Prospective matching	Examine precipitating factors for delirium during hospitalization. Two prospective cohorts of consecutive patients aged 70 years and older admitted to general medical service n = 196 first cohort	Develop and validate a predictive model for delirium based on noxious insults or factors occurring during hospitalization >25 candidate risk factor variables studied		Study demonstrated distinct risk gradients, with patients placed in low, intermediate, or high-risk groups showing a statistically significant trend towards increasing risk of delirium with increasing numbers of precipitating factors.
university hospital Study Length/Start-Stop Dates Not discussed	strategy to assure comparability of patients between intervention and control groups	n = 312 second cohort Inclusion Age ≥ 70 -admitted to general medicine	Precipitating factors Use of physical restraints Malnutrition More than 3 medications added Use of bladder catheter	RR 4.4 (2.5 – 7.9) RR 4.0 (2.2 – 7.4) RR 2.9 (1.6 – 5.4) RR 2.4 (1.2 – 4.7)	RR for delirium increased from 1.0 in the low-risk group to 22.7 i the high-risk group. -validated in the second cohort o patients which produced similar,
Purpose To describe the multifactorial etiology of delirium; to elucidate the predisposing and precipitating factors for delirium derived from earlier work; and to present an overview of the Delirium Prevention Trial, which was targeted to address delirium risk factors.	Protocols for targeted risk factors Cognitive impairment -reality orientation -therapeutic activities Sleep deprivation -noise reduction -uninterrupted slep Immobility -early mobilization -minimize immobilizing equipment Visual impairment	service at a university hospital Intervention group = 426 Delirium Prevention Trial Intervention (Hospital Elder Life Protocol) Intervention (see Protocols for targeted risk factors) Standardized protocols targeted towards six delirium risk factors. Delirium assessment: Assessment tool: CAM	Any iatrogenic event Incidence of delirium Days of delirium Total no. episodes of delirium Rate of adherence to all intervention protocols Adherence rate for individual intervention protocols Intervention resulted in a significant reduction in the total number of risk	RR 1.9 (1.1 – 3.2) Intervention vs. control 9.9% vs. 15% OR .6 (0.39- .92) 105 vs. 161 p = 0.02 62. vs., 90 p = 0.03 87% 71% - 96%	statistically significant risk gradients. No adverse effects were associated with any intervention protocols Through the identification of risk factors and targeting intervention strategies towards them, we have been successful in preventing delirium in hospitalized older patients, reducing the risk of delirium by 40%.
Funding source(s): Grants from NIA and Patrick and Catherine Weldon Donaghue Medical Research Foundation	-vision aids -adaptive equipment Hearing impairment -amplifying devices -hearing aids -wax disimpaction Dehydration	All patients assessed daily by RAs who had no role in the intervention unaware of intervention or study group assignment	factors per patient compared with the usual care group at reassessment Improvement in the orientation score of patients with cognitive impairment at admission	p = 0.001 40% vs 26% improved; p = 0.04	Results suggest that primary prevention of delirium, (preventin delirium before it occurs), may be the most effective treatment strategy for delirium, a finding which holds substantial clinical and health policy implications for
<b>Quality Score</b> : 7 <b>Risk of Bias</b> : Unclear	-early recognition -volume repletion	<b>Control Group = 426</b> Protocol = Usual care with daily delirium assessment	Reduction in the rate of use of sleep medications in all patients	46% vs 35%; p = 0.001 NOTE: Specific recommendations for delirium prevention detailed in PDF	delirium management in specific and for the geriatric population more generally.

of delirium by 40%.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not discussed
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-Holt R, Young J, Heseltine D. Effectiveness of a multi-component intervention to reduce delirium incidence in elderly care wards. Age Ageing. 2013;42(6):721-7.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Other Information
Holt 2013 Jnited Kingdom	Before group N = 1123 admitted to study wards	n = 149 before group (10/2007 to 3/2008)	Delirium assessment: MMSE CAM(4-tem)	Delirium assessed daily by trained research assistants using CAM, DRS-R-98	Delirium incidence, duration and severity were all
<b>Setting</b> Specialist acute	After group N = 1039 admitted to study	n = 210 analyzed n – 3 Lost to follow up	DRS-R-98	-assistants blind to baseline assessments	significantly reduced durin the intervention
derly care wards at	wards	n = 207 analyzed at 6 mo follow		-inter-rater reliability was monitored	implementation phase of
general hospitals	Inclusion	up.		4 weeks during the study	the study.
Study Design	Inclusion Patients with acute	Men and women (65.7%)	Baseline characteristics	Before group vs. after group	The reduction in delirium
Pre/post study	medical illness admitted from Accident and	Mean age 85 (6.01)	Gender (% male) Resident in LTC prior to admission	34.3% vs. 50% p = 0.003 13.3% vs. 4.6% p = 0.006	persisted after adjustmen for differences in baseline
Selection method	Emergency department or	Protocol	Dehydration urea/creatinine ratio >	68.1% vs. 77.6% p = 0.046	delirium risk and
Patients admitted to	directly by general	Usual care (Comprehensive	0.073		demographic variables.
one of three specialist	practitioners to one of	Geriatric Assessment and	Hearing impairment	59% vs. 71.7% p = 0.013	0 1
elderly care wards	three specialist elderly	multidisciplinary care)			Process outcomes
	care wards		Primary outcomes	Before group vs. after group	Delirium education sessio
Study Length/Start-		Baseline assessments (all	Patients developing incident		attendance: 70% of staff
Stop Dates 0/2007 – 1/2009	Exclusion (before group) N = 907	patients)	delirium during first 7 days after admission to study ward	13.3% vs. 4.6% p = 0.006	Healthcare assistants and
0/2007 - 1/2009	n = 33 prevalent delirium	Demographics Dehydration	Adjusted for baseline imbalances	OR $3.665(1.40-9.591)$ p = 0.008	staff nurses who had
Purpose	at baseline	Creatinine	Adjusted for baseline imbalances	Or 3.003(1.40 3.331) p = 0.000	increased knowledge abo
o examine the effect	n = 752 too unwell to be	Acute illness severity	Secondary outcomes		delirium: 82%
f a multi-component,	assessed (in the opinion of	Comorbidity	Duration of delirium during first 7	0.29 days (.931) vs. 0.06days(2.87)	
elirium prevention	clinical staff)	Medications	days	p = 0.002	Recorded adherence to
ntervention on rates	n = 122 unable to	Mobility	Severity of delirium during first 7		delirium risk factor
of incident delirium for	communicate (dysphasia,	Visual or hearing impairment	days	16.86(4.92) vs. 9.17(7.94) p = 0.005	modification protocols: (2
patients admitted to pecialist elderly care	unable to speak English) or obtain consent within 24	Cognitive impairment (MMSE) CAM – 4 item version	Hospital readmission w/in 6 mo following discharge	41.1% vs. 54.1% p = 0.02	57%)
vards	h of ward admission	DRS-R-98	Process outcomes	41.170 vs. $54.170$ p = $0.02$	Protocol adherence was
				see Other Information Column	highest for reorientation a
	Exclusion (after group)	n = 187 after group (8/2008 to	Delirium assessment:	See above	hydration, and lowest for
Funding source(s):	N = 884	01/2009			mobility and constipation.
Research grant from	n = 32 prevalent delirium		Baseline	See above	
Research into Ageing	at baseline n = 758 too unwell to be	n = 152 analyzed	characteristics/measures	See above	
Quality Score:	assessed (in the opinion of	n = 4 lost to follow up n = 148 analyzed at 6 mo. follow	Primary outcomes	See above	
	clinical staff)	up		See above	
	n = 94 unable to	~P	Secondary outcomes		
Risk of Bias:	communicate (dysphasia,	Men and women (50%)	-		
High	unable to speak English)	Mean age 85.8 (5.39)			
	or obtain consent within 24	Drata a d			
	h of ward admission	Protocol Usual care plus delirium prevention			
	Delirium risk factors	intervention:			
	targeted	(1) Identification of local opinion			
	Disorientation	leaders or 'champions' to lead the			
	Dehydration	implementation of the intervention.			
	Visual/hearing impairment	(2) An initial educational			
	Constipation	intervention to raise awareness,			
	Pain Immobility	knowledge and enthusiasm.			
	Immobility	(3) A practice change intervention directed at delirium risk factors.			
(av Points: 1) Delirium	is common in older people ad		2) It is uncertain if multi-component d	L elirium prevention interventions reduce i	ncident delirium on speciali
Toy ronus. I) Denillull	na common in older people ad		ent prevention intervention on elderly ca		noident deimann on speciali

Conclusion: A multi-component, delirium prevention intervention directed at delirium risk factors and implemented by local clinical staff can reduce incidence delirium on specialist elderly carge wards.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Significant differences between groups
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Pre/post design
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	RAs only blinded to baseline assessment, not outcome assessments
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Low	Pre/post design; historical controls Potential confounding variables due to changes in practice not recorded by the study team that may have affected rates of delirium
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

### G3-Martinez FT, Tobar C, Beddings CI, et al. Preventing delirium in an acute hospital using a non-pharmacological intervention. Age Ageing. 2012;41(5):629-34.

Otente	Demoletien		Res	-l	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Martinez 2012	N = 1285 eligible	n = 144 Intervention group	Delirium assessment:	CAM administered daily by	Lost to follow-up (all analyzed
Chile	n = 294 did not meet		CAM	three trained observers who	n = 4 in intervention group
	inclusion criteria	Men and women (42%)	-	had validated each other to	n = 9 in control group
Setting	n = 287 randomized	Mean age 78.1 (6.3)		Fleiss kappa statistic (K = 1)	
nternal medicine				-Observers did not diagnose	
vard at a hospital	Inclusion	Protocol		cognitive impairment and	The most important difference in
varu al a nospilai	Patients with at least one	Carried out by patient's family:			outcomes was a moderate
		Carned out by patient's family.		dementia diagnosed based	
Study Design	risk factor for delirium from			solely on chart review	tendency towards a delayed
Single blind	a clinical prediction rule:	(i) Education: the observers conducted			onset of delirium in our study,
Randomized	-Age > 70	brief interviews with each patient's	Baseline characteristics	No significant differences	which could also be a
controlled clinical trial	-Hx cognitive impairment	family members, in which the main			consequence of the non-
	documented and MMSE <	aspects regarding the clinical features		Intervention vs. control	pharmacological intervention.
Randomization	24 prior to hospitalization	and prognostic implications of acute	Primary outcomes	N = 144 vs 143	
nethod	-alcoholism or metabolic	confusional syndromes were explained.	Incident delirium	5.6% vs. 13.3%	The incidence of dementia was
Computer-generated	imbalances at moment of	These interviews lasted no more than		RR $0.41(0.19-0.92)$ p = 0.027	low, roughly affecting 6% of the
andom numbers	admission	10 min overall and were accompanied		RR reduction of developing	included patients, as was the
andom numbers	aumission				
		by a specially designed pamphlet.		delirium 59%	prescription of high-risk
Study Length/Start-	Exclusion		(breakdown by type)		medications during the hospital
Stop Dates	N = 704	(ii) Provision of a clock (analogue or	Mixed delirium	1.4% vs. 6.3%	stay, present in just about the
9/2009 – 6/2010	n = 434 not hospitalized in	digital as required by the patient) and	Hypoactive delirium	1.4% vs. 5.6%	same proportion (5%). Both
	general ward	calendar in the room.	Hyperactive delirium	2.8% vs. 1.4%	these findings are surprising,
Purpose	n = 181 placed in a room				considering the important role
To determine whether	with more than 2 beds (to	(iii) Avoidance of sensory deprivation			that they play as predisposing
a non-	prevent interference w/	(glasses, denture and hearing aids	Secondary outcomes		and triggering factors of delirium
pharmacological	non-pharm intervention)	must be available as needed).	Falls	0% vs. 2.8% p = 0.06	respectively, and should be kep
		must be avaliable as needed).	Falls	0% vs. 2.8% p = 0.00	
ntervention delivered	n = 23 family members				in mind when analyzing results.
by family members	unavailable	(iv) Presence of familiar objects in the			
could reduce the	n = 11 declined to	room (photographs, cushions and			Reasons could be:
ncidence of delirium,	participate	radio).			-patients with present delirium
as compared with	n = 6 safety reasons				excluded from study
standard	n = 15 delirium at initial	(v) Reorientation of patient provided by			-patients with moderate to
management of	visit	family members (current date and time,			advance stages of dementia are
elderly inpatients at	n = 34 not	recent events).			admitted to special care wards
ntermediate or high	randomized/earthquake				not suitable for study
risk of developing this	Tanuoniizeu/eariinquake	(vi) Extended visitation times (5 h			comparisons
	Delinium nick festens				compansons
condition during the	Delirium risk factors	daily).			
course of	Age >70				
hospitalization.		n = 143 control group	Delirium assessment:	See above	
	Previous history of				
Funding source(s):	cognitive impairment in	Men and women (33%)	Baseline characteristics	See above	
Not discussed	medical record (MMSE	Mean age 78.3 (6.1)			
	<24		Primary outcomes	See above	
Quality Score		Protocol	i initiar y outcomes		
5	Alcoholism		Secondary outcomes	Saa ahaya	
)	Alcoholisti	Usual care	Secondary outcomes	See above	
Risk of Bias:	Metabolic imbalances				
	Metabolic impalances				
High					
(av Points: 1) Delirium	is a common neuronevehistric	syndrome that is most frequently seen in t	 elderly nationts 2) It has been asso	ciated with increased morbidity of	I mortality functional impairment
		n this study, a multicomponent intervention			
npatients.		n and study, a manuomponent intervention	active by family members sign		is in a group of clucity medic
	hormonological intervention	arried out by family members reduced the r	iok of doveloping deliving in a dis-	to in general modifies words. The	abaan ad NNT of 40 makes 't
	onarmacological intervention C	amed our by family members reduced the r	isk of developing delifium in Datien	is in deneral medicine wards. The	ODSERVED ININ LOT 1.3 MAKES IT

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	1	Low	
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observers not blind to allocation group
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observers not blinded to outcome assessment
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Intervention was carried out by family members who could have implemented other measures that may have influenced delirium development
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G3-G5-Rubin FH, Williams JT, Lescisin DA, et al. Replicating the Hospital Elder Life Program in a community hospital and demonstrating effectiveness using quality improvement methodology. J Am Geriatr Soc. 2006;54(6):969-74

C 4 u d	Denulation	Intervention Onever		Results	Correcto
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
RubinFH 2011	N = 1929	n = 704 HELP Intervention	Delirium assessment:	A nurse practitioner evaluated patients	
JSA	n = 1225 baseline (pre-	Time period: 7/2002 – 12/2002	Specific assessment tools	for the presence of delirium and for the	Factors contributing to success
	intervention)		not described	presence of modifiable predisposing or	Shadyside included
etting	n = 704 post	Men and women (63.5%)		precipitating factors. She interacted with	-a long tradition of QI
community teaching	intervention	Mean age 80.9 (6.7)		staff nurses and treating physiciabns.	improvements for elderly
ospital				······································	inpatients;
•	Inclusion	Phase in data collected 1/2002			-inclusion of all stakeholders in
tudy Design	Aged ≥ 70	through 6/2002	Baseline characteristics	Significant difference between groups	the project, especially nursing a
re-test/post-test quality	Admitted to Hospital	5		Baseline vs HELP	ancillary personnel, so that
nprovement study	Elder Life	HELP implementation 7/2002-	Cerebrovascular disease	7.4% vs 3,7%, p .001	concerns of competition or "tur
		12/2002	Gastrointestinal disease	5.1% vs 12.4%, p <.001	were resolved at the outset;
election method	Exclusion		Ischemic heart disease	2.7% vs 4.5%, p .04	-an accompanying educationa
Patients admitted to a	N = not discussed	Protocol	Renal failure	0.4% vs 1.4%, p .03	campaign to generate support;
ursing unit	-Diagnosis of	Hospital Elder Life Program			-an identified senior physician
alonig and	schizophrenia	Daily interventions targeted	Primary outcomes	Baseline vs. Intervention	champion;
Study Length/Start-	-Baseline use of major	patients were not delirious and	Delirium rates	40.8% vs. 26.4% p < .002	-use of data that hospital
Stop Dates	tranquilizers	who were at intermediate risk for	Bointan Tatoo	10.070 VO. 2017/0 p 3.002	leadership found credible;
2001 - 2002	aanquiizoro	developing delirium			-agreement with management
2002		ao cooping aomain	Financial outcomes		the outset on what outcomes
urpose	HELP Implementation	Risk factors present:	Est 101 cases prevented	\$220,281 cost savings	would be important;
o evaluate a replication	personnel	-cognitive impairment	14.4% reduction in delirium	\$220,201 000t 00ving0	-beginning with only one unit;
f the Hospital Elder Life	-Elder life specialist	-sleep deprivation	rate	364 bed-days saved	-institution-wide celebration of
Program (HELP), a	(1.0 FTE)	-immobility	Net cost savings (cost		results.
juality-improvement	-clinical geriatrician	-visual or hearing impairment	savings –cost of		
nodel, in a community	(0.1 FTE)	-dehydration	HELP)	\$562,611 in 6 mos on one 40-bed	
nospital without a	-geriatric nurse	achyaration	11221 )	nursing unit	
esearch infrastructure.	practitioner (0.5 FTE)	Deviations from the original	Nursing satisfaction		
ising administrative data		HELP model	outcomes		
		-exercise and fluid repletion	Nurses and nurses' aides		
		protocols omitted due to	Agreed	"My job is more satisfying due to HELP"	
Funding source(s):		insufficient staffing	Highly agreed	"It would be helpful to make HELP a	
hadyside Hospital		-sleep protocol modified	riiginy ugreed	permanent program on my unit"	
oundation funded the		-the Role of the nurse		permanent program on my unit	
Shadyside replication.		practitioner was modified to	Patient satisfaction with		
he HELP dissemination		eliminate redundancies with	HELP	2.8/3 rating for overall satisfaction	
effort was funded in part		existing services	11221		
by grants from the		existing services			
National Library of					
Nedicine, the Commonwealth Fund		n = 1,225 Baseline (control)	Delirium assessment:	See above	1
		Time period: 1/2001 – 12/2001			
he Fan Fox and Leslie			Baseline characteristics		
R. Samuels Foundation),		Men and women (63.8%)		See above	
and the Retirement Research Foundation.		Mean age 80.6 (6.2)	Primary outcomes		
Research Foundation.				See above	
Quality Coores		Baseline data measured	Secondary outcomes		
Quality Score:		throughout 2001	coordinary outcomos	See above	
}					
Nek of Blood Link		Protocol			
Risk of Bias: High		Standard care			
	1			1	1

Conclusion: Conclusion: HELP can be successfully replicated in a community hospital, yielding clinical and financial benefits

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Individuals not randomized or individual matched. Differences between groups
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Allocation not concealed due to different time periods
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Outcome assessors not blinded
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Pre/post design Cohorts were assessed at different time periods and thus there may be other confounding variables
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	0		Delirium assessment tool not described
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on <u>the criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

G3-Bjorkelund KB, Hommel A, Thorngren KG, et al. Reducing delirium in elderly patients with hip fracture: a multi-factorial intervention study. Acta Anaesthesiol Scand. 2010;54(6):678-88

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Bjorkelund KB 2010	N = 478 assessed for	n = 139 Intervention (admitted	Delirium assessment:	Post-op, patients were tested a minimum	Adverse effects
Sweden	eligibility	after 10/1/2003)	SPMSQ	of 8h after the end of anesthesia and	No significant difference
weden	n =139 excluded	n=8 excluded	OBS	daily by 2 researchers. Patients showing	between groups other that
- 441				, ,	
etting	n = 1 denied participation	n=2 no operation	DSM-IV	signs of delirium when tested with the	delirium
Jniversity Hospital	N = 276 eligible	n=6 Hx/treatment of previous		OBS scale or were reported as delirious	
	n = 139 intervention	delirium, dementia		by the nurse were evaluated in relation to	Differences in pre- intra-
Study Design	n = 136 control	n = 131 analyzed		the DSM-IV criteria of delirium on a later	and post-operative data
Prospective,		······ <b>·</b> ······ <b>·</b> ····················		occasion by a psycho-geriatrician	(see data Table 4)
•	Inclusion	Men and women (71%)		occasion by a psycho-genatician	Significant differences
opulation-based,					
uasi experimental	-Age ≥ 65	Mean age 81.1 (7.5)			-SpO2 preop, <0.0001
tudy	-Assessed as cognitively		Baseline characteristics	Significant differences:	-SpO2 Day 2, <0.0001
	intact at admission	Protocol (initiated 10/1/2003)		Intervention vs. Control	-heart rate lowest, 0.043
election method	-SPMSQ ≥ 8	Screened for cognitive impairment	Walking ability	84% vs. 93.9% p=.036	-Body temp, 0.004
Consecutive patients		within 30 min after admission to the	Use of diuretics	31.3% vs. 47% p=.009	-i.v. fluid preop, <0.0001
	Exclusion				
dmitted with hip		ED using the SPMSQ and within 4	S-sodium(m/mol)	142(139-144) vs.141(138-143) p=.047	-i.v. fluid postop, 0.001
acture	N = 139 total	h for delirium and daily thereafter	S-potassium(m/mol)	3.8(3.6-4.1) vs. 4 (3.7-4.3) p=.013	-analgesics RR, 0.009
	n = 35 Age < 65	using the OBS			-antiemetics (anesthetic
tudy Length/Start-	n = 104 for	Other multi-factorial program	Delirium outcomes	Intervention vs control	period), <0.0001
top Dates	-SPMSQ < 8	components:	Delirium during hospitalization	22.1% vs. 34.1% p=.031	-admission Orth ward
/2003-4/2004	-History of cognitive	1. Supplemental oxygen 3-4l/min	Post-operative delirium	21.4% vs. 33.3% p=.030	preop, <0.0001
/2003-4/2004	, ,				preop, <0.0001
	impairment,	2. Intravenous (i.v.) fluid	Developed hypoxia	9.8% vs. 20% p=.026	
urpose	-Severe	supplementation and extra nutrition			Limitations
o investigate whether	neuropsychiatric illness,	<ol><li>Increased monitoring of vital</li></ol>	Significant risk factors	Delirium % vs no delirium %, p	<ul> <li>-use of quasi-experiment</li> </ul>
n implementation of a	-Communication	physiological parameters	Age ≥ 80	89.7% vs 48.0% <0.0001	design
nulti-factorial program,	difficulties	4. Adequate pain relief	Institutional care	31,.0% vs 7.8%, 0.003	-unable to change the w
ncluding intensified	-Multi-trauma	5. Avoid delay in transfer logistics	Need walking aids	69.0% vs 38.2%, 0.003	patients were located in
0	-iviulu-u autita		•		•
re-hospital and		6. screen for delirium through daily	SPMSQ score 8 or 9	86.2% vs 33.3%, <0.0001	hospital (admitted to
erioperative treatment	Cognitive/Delirium	testing with the OBS scale	Neurological diagnosis	37.9% vs 17.6% 0.020	available bed)
ind care could reduce	Assessment	<ol><li>Avoid polypharmacy</li></ol>	Rx drugs ≥4	79.3% vs 51.5%, 0.008	-no blinding of clinical
ne incidence of	Short Portable Mental	8. Standard protocols for	Rx diuretics	51.7% vs 25/5%, 0.007	personnel who had to be
lelirium in elderly	Status Questionnaire	-premedication, anesthesia,	Rx nitroglycerine	20.7% vs 2.9%, 0.004	trained to deliver the
,	(SPMSQ)	monitoring, blood loss/transfusion,	Rx anticholinergic		protocols
atients with hip					•
racture and cognitively	Organic Brain Syndrome	Sedation, postoperative analgesia	Cardiac failure	13.8% vs 2.9%, 0.042	-presence of pain or tx
ntact at admission.	Scale (OBS)		BOLD = significant		with opioids may have
			intervention and control		influenced initial SPMSQ
unding source(s):		n = 136 Control (admitted before	Delirium assessment:	Not described	score and affected
Swedish National		10/1/2003)	Significant risk factors	Delirium % vs no delirium %, p	exclusion of some patier
Board of Health and		,			-researchers not blinded
		n = 4 excluded	Female	55.6% vs 77.0%, 0.011	
Velfare, the Swedish		n = 1 no operation	Male	44.4% vs 23.0%, 0.011	the use of the OBS which
ssociation of Local		n = 3 Hx/treatment of previous	Age ≥ 80	88.95 vs 51.7% <0.0001	may have influence the
uthorities and		delirium, dementia	Impaired hearing	64.4% vs 32.2%, <0.0001	reliability of the
legions, HSF, Council			Need walking aids	66.7% vs 41.4%, 0.006	assessments
or Medical Health Care		Men and women (69.7%)	SPMSQ score 8 or 9		
lesearch in Southern					
		Mean age 82(7.6)	ASA III + IV	51.1% vs 24.1%, 0.002	
weden			Rx anticholinergic		
		Protocol	S-hemoglobin <6.2 (mmol/l	13.3% vs 1.1%), 0.006	
uality Score:		Usual care	S-potassium >4.7 (mmol/l))	11.4% vs 2.4%, 0.045	
•			S creatinine >100 (µmol/l)	33.3% vs 13.8%, 0.008	
			Blood transfusion <2U	*	
liak of Rise:					
lisk of Bias:			Cardiac failure		
ligh			Myocardial infarction		
			Death within 30 days of	8.9% vs 0, 0.012	
			surgery		
	1	1		l elderly hip fracture patients, lucid at admissic	1

delirium during hospitalization from 34% to 22%.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouve et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences between groups at baseline
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Quasi-experimental design (before/ after implementation of intervention program)
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Study design – no blinding
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Exclusions/dropouts after group assignment (<10%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Problematic study design (historical controls; before/after study) Baseline imbalances Possible confounders
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G3-Vidan MT, Sanchez E, Alonso M, et al. An intervention integrated into daily clinical practice reduces the incidence of delirium during hospitalization in elderly patients. J Am Geriatr Soc. 2009;57(11):2029-36

Study	Population	Intervention Groups	Measure	Results Outcome	Comments
Characteristics	Fopulation	intervention Groups	weasure	Outcome	Comments
Vidan MT 2009	N = 1,027 eligible	n = 170 Intervention	Delirium assessment:	A trained RA tested each delirium	
	n = 904 screened	(geriatric unit)	CAM		Adherence
Spain	n= 362 excluded (most	(genatric unit)	CAM	criterion daily (every morning) in all	
Dettine a				patients using a structured interview.	Overall rate of adherence was
Setting	because of severe	Men and women (62.4%)		To detect delirium episodes in the	75.7% of patient-days per
University Hospital	dementia)	Mean age 85.9 (6)		afternoon and evening or at night, a	intervention actions, with the
	-140 excluded			family member and the attending nurse	highest rate in mobilization (919
Study Design	intervention group	Protocol		were interviewed daily, and the medical	and the lowest in sleep
Controlled clinical trial	<ul> <li>-222 excluded control</li> </ul>	-Quality improvement		records were reviewed.	preservation (50%).
	group	program with two major			
Selection method	N = 542 included and	components:	Baseline characteristics	Intervention vs. Control	
Consecutive patients	analyzed	1. An educational program	Age	85.9 vs. 82.1 p<.001	The intervention was also
admitted to geriatric	-	aimed at changing the	Female	62.4% vs. 53% p=.04	successful at improving other
acute unit and internal	Inclusion	approach of geriatric ward	Widowed	64.7% vs. 51.8% p=.01	parameters that can be
medicine wards	Age ≥ 70	staff to patient care	Living at home before admission	77.2% vs. 85.7% p=.01	considered quality indicators in
	-Admitted to geriatric	2. A set of specific targeted	# basic ADLS performed	3,28(2.1) vs. 3.8(1.9) p=.02	the management of elderly
Study Length/Start-	acute care unit	actions in seven risk factor	any impairment in ADLS	78.8% vs. 73.4% p=.04	hospitalized patients.
Stop Dates	-Admitted to two internal	domains	independent ambulation	35% vs. 51% p=.001	
1/2007-12/2007	medicine wards	domanio	mean MMSE score	20.8(6.7) vs. 21.8(6.5) p=.04	The use of glasses and hearing
1/2007-12/2007	-Had at least one of four	Started in the first 24 h of	Hearing impairment	64% vs. 45.9% p=.001	aids increased in patients who
Durnaaa		admission as part of	0 1		needed them, as did the rates of
Purpose	risk factors of delirium		High risk of delirium	44% vs. 29% p=.001	
To analyze the	<ul> <li>cognitive impairment,</li> </ul>	standard clinical practice by			daily mobilization, and the use
effectiveness of a	- visual impairment,	all clinical staff	Primary outcomes		physical restraints was reduced
multicomponent	-acute disease severity		Incidence of delirium	11.7% vs. 18.5% p=.045	
intervention integrated	-dehydration)	The specialist geriatric nurse		No significant difference	
into daily practice for		coordinated nursing	Mean intensity of delirium (0-7)	4.9 (0.4) vs 5,3 (1,.0), p=.08	In addition, the intervention
the prevention of in-	Exclusion	interventions.	Length of delirium episode (h)	32.1 (43.0) vs 33.6 (22.0), p=.73	increased the number of patien
hospital delirium in	N = 362		Patients with >1 episode (n)	0/20 vs 6/69, p=.22	taking daily mobilization
elderly patients	-Delirium at time of	Most actions were performed	Functional decline in delirium		exercises and reduced the rate
5.	admission	daily in all patients, and	patients	60% vs 71.2%, p=.41	functional decline without an
Funding source(s):	-Presence of severe	others, such as interventions	Intermediate risk for delirium	6.3% vs 15.2%. p=.03	increase in the incidence of falls
Grant from Spanish	dementia that impaired	involving hydration and	Mortality	2/20 vs 10/69, p=.60	during hospitalization, suggesting
Geriatrics Society,	communication	nutrition, were performed	Functional decline	45.5% vs. 56.3% p =.03	that the program is safe.
Public Grant from	-Aphasia of any origin	only if necessary.		10.070 VO. 00.070 p .000	and and program to date.
Fondo de	-Coma	only in necessary.	Subgroup analysis matched for	Delirium incidence =	
	-Agnoic status	Adherence was monitored	age and risk factor	11.3% vs. 21% p=.01	
Investigacion	0		age and tisk factor	11.3% vs. 21% p=.01	
Sanitaria-Instituto de	-expected hospital LOS	using a checklist of actions	La sistia na succesia a fan		
Salud Carlos II	< 48 h	evaluated every day for each	Logistic regression for		
		member of the sample.	significant risk factors		
Quality Score	Assessments		Dementia	2.14 (1.15-3.99), p=.02	
4	CAM		Baseline ADL independence	0.78 (0.69-0.89), p=.001	
	ADLs		In hospital stay (per day)	1.02 (1.00-1.05), p=.05	
Risk of Bias:	Functional Ambulation		Intervention group	0.43 (0.24-0.77), p=.005	
Unclear	Classification (mobility)				
	APACHE II				
	Charlson Comorbidity	n = 372 Control (internal	Delirium assessment:	See above	
	Index	medicine units)			
	MMSE	,	Baseline characteristics	See above	
		Men and women (53%)			
		Mean age 82.1 (6)	Primary outcomes	See above	
		Brotocol			
		Protocol			
		Usual care			
<b></b>					
	anaa at daliriym dyring haanit	hization in alderly notionts can be	a reduced with an intervention proto	col aimed at reducing the number of precipit	ating tactors and improving the

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Many baseline significant differences between groups
2. Allocation concealment (1 point if achieved):			
<ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul>	0	Unclear	Patients assigned to different wards, but potential for nursing staff to work on both wards
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	No blinding, but attempts to conceal allocation
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Used ITT to evaluate intervention effectiveness and baseline characteristics with potential confounding effects included in logistic regression analysis and secondary subgroup analysis using matched controls
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-G5-Inouye SK, Bogardus ST, Jr., Baker DI, et al. The Hospital Elder Life Program: a model of care to prevent cognitive and functional decline in older hospitalized patients. Hospital Elder Life Program. J Am Geriatr Soc. 2000b;48(12):1697-706

Study	Program Personnel	Program Description	Measure	oults Outcome	Comments
Characteristics	Flogram Fersonner	Program Description	Measure	Outcome	comments
Inouve SK 2000	N = approximately 800	Enrollment criteria	Quality assurance procedures		The HELP program is
JSA	patients/year in 2000 (200-250	Inclusion	Adherence (overall rates for all	Adherence rates:	unique in its hospital-wid
JOA	patients at start up)	Age ≥70	interventions)	89% for 37,131 patient-days	focus, provides skilled
Potting	patients at start up)	$\geq 1$ risk factor for cognitive or functional	Non adherence	09% 101 57, 151 patient-days	
Setting	Due anno 1	5		00%	staff, including trained
General medicine	Program personnel	decline	Staff/volunteers not available	32%	volunteers, to provide
service at urban	-Elder Life Nurse Specialist	-MMSE ≤24	Patient refusal	26%	interventions to all
university hospital	-Elder Life Specialist/	-mobility or ADL impairment	Medical contraindication	22%	patients.
	Volunteer Coordinator	-Dehydration	Patient unavailability	13%	
Study Design	-Geriatrician	-Vision impairment			A dedicated geriatric uni
QI Evaluation of	-Program Director	-Hearing impairment	Program benefits	Intervention vs control	is not required
HELP implementation	_	Able to communicate verbally or in	MMSE	8% decline in MMSE 2+ points	
·	Volunteers	writing		vs. 26% in controls	A unique strength of the
Selection method	-carry out core interventions	Exclusion		(proportionate increment=0.69)	program is the targeting
NA	-rigorous selection criteria	Coma	ADL	14% decline in ADL 2+ points	common, modifiable,
	-extensive training	Mechanical ventilation	, (BE	vs. 33% in controls	evidence-based risk
Study Length/Start-	-didactic and small group	Aphasia		(proportionate increment=0.58)	factors that are relevant
	<b>3</b>			(proportionate increment=0.50)	
Stop Dates	-one : one on wards	Combative/dangerous behavior			older hospitalized patien
3/1995-8/1999	-weekly shift commitments	Severe psychotic disorder	Ongoing HELP Outcomes	7 1 (1 100 1)	using interventions to be
_	-minimum 6 month program	Severe dementia (case by case)	Median LOS	7 days (1-163 d)	feasible and generalizat
Purpose	commitment	Respiratory isolation	Discharged to home	56%	to other settings.
To describe the	-must meet competency	Discharge within 48 hours	Discharged to short-term		
Hospital Elder Life	evaluation by Elder Life	Refusal by patient, family, physician	rehabilitation in nursing home	15%	Effectiveness of the
Program, a new	Specialist before initial patient	Other (documented)			program has been
model of care	contact		Sleep Protocol Effectiveness		demonstrated through
designed to prevent	-quarterly competency checks	HELP Intervention	Protocol adherence	74% adherence; no adv effects	research studies for
functional and	-retention enhanced	Goals:	Reduction in sedative use	54% vs. 31% (p< .02)	prevention of delirium ar
cognitive decline of	-staff communication	(1) to maintain physical and cognitive			cognitive and functional
older persons during	-educational sessions	functioning throughout hospitalization;	Other Program Benefits		decline.
hospitalization.	-support groups	(2) to maximize independence at	ether rogram zeriente		decime.
nospitalization.	-monthly newsletter	discharge;	Reduced overall hospital costs		The HELP program is
	-recognition incentive awards	(3) to assist with the transition from	Reduced overall hospital costs		readily adaptable to othe
Funding source(s):	-recognition incentive awards		Community porception of high		
CCT funded by		hospital to home; and (4) to prevent	Community perception of high		hospital settings.
private foundation	Interdisciplinary expertise	unplanned readmission.	quality geriatric care		<b>5</b> · · · · · · · ·
grants and NIA	Consultation and support to the				Barriers to implementation
Yale New Haven	program	Core interventions	Geriatric education/expertise		in other settings
Hospital assumed	-geriatric nurse practitioners	Carried out by program staff and	resource		-institutional support for
funding for the	-geriatric chaplaincy	volunteers			start up personnel and
program as a	-clinical pharmacy	-protocols for daily visitor/ orientation	Program Costs	200-256 patients/year	equipment
permanent hospital	-nutrition	-therapeutic activities			-changing ingrained
program in January	-rehabilitation therapies	-early mobilization	Equipment and supplies	\$3,000 (startup) for 1-2 units	geriatric practices
1998.	(physical, occupational,	-vision/ hearing	Average daily census	4-5 patients	-developing support fro
	recreational)	-oral volume repletion	Intervention visits/day	12-15 (per 3xday protocols)	key nursing and physicia
Quality Score	-care coordination	-feeding assistance,	Staff effort	1.6 to 1.7 FTEs	personnel
5	-social work	-sleep enhancement.	Minimum volunteers	21 (1 shift/week)' 6 patients/shift	-ongoing clinical
5			Consultants	Costs not included in program	0 0
Diak of Diac	Administration	-geriatric nursing assessment and	Consulations		personnel training
Risk of Bias:	Administration	intervention		budget	-frequent turnover of
Unclear	-HELP Working Group	-interdisciplinary rounds			personnel
	-Program Director/	-provider education program			-recruitment (extensive
	Geriatrician	-community linkages and telephone			training and retention of
	-nurse specialists	follow-up			volunteers
	-Elder Life specialists	-geriatrician consultation			
	-Community Advisory Board	-interdisciplinary consultation			

**Conclusion**: These results suggest that the Hospital Elder Life Program successfully prevents cognitive and functional decline in at-risk older patients. The program is unique in its hospital-wide focus; in providing skilled staff and volunteers to implement interventions; and in targeting practical interventions toward evidence-based risk factors. Future studies are needed to evaluate cost-effectiveness and long- term outcomes of the program as well as its effectiveness in non-hospital settings.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouve et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Unclear	Not applicable
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ol> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ol>	0	Unclear	Not applicable
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Non-concurrent controls from prior RCT
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G3-G5-Lundstrom M, Olofsson B, Stenvall M, et al. Postoperative delirium in old patients with femoral neck fracture: a randomized intervention study. Aging Clin Exp Res. 2007;19(3):178-86.

				Results	<b>•</b> .
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Lundstrom M 2007	N = 353 patients	n = 102 Intervention	Delirium assessment:	Delirium assessments by study nurses	Multivariate linear regression
Sweden	assessed for eligibility	n = 6 patients died during	MMSE	daily postop days 1-7; blinded specialist	to control for baseline
	n = 154 excluded	hospitalization	Organic Brain Syndrome Scale	in geriatric medicine analyzed all	differences
Setting	N = 199 randomized	n = 92 assessed at 4 months	(OBS)	assessments and documentation once	Dependent variable = number
University hospital	and analyzed	n = 86 assessed at 12 months	DSM – IV	during hospitalization	of days with postop delirium
					Independent variables (p)
Study Design	Inclusion	Men and women (72.5%)			-delirium post op (<0.001)
RCT	-Age ≥ 70	Mean age 82.3 (6.6)	Baseline characteristics	No significant differences, except:	-control group (0.001)
	-Consecutively admitted			Intervention vs. Control	-male sex (0.004)
Randomization method	to Orthopedic	Protocol	Depression	32.4% vs. 47.4%, p 0.031	-depression (NS)
Sealed envelope.	Department	-Patients randomized to the	Antidepressants	28.4% vs.46.4%, p 0.009	-dementia (NS)
Stratified according to	-Femoral neck fracture	intervention group were			-age (NS)
dislocation of fracture.		admitted to a 24-bed geriatric	Primary outcomes	Intervention vs. Control	
	Exclusion	unit specializing in geriatric	Days postoperative delirium	5.0 (7.1) vs. 10.2(13.3) p =0.009	Despite some baseline
Study Length/Start-	N = 154	orthopedic patients.	Patients delirious postop	54.9% vs. 75.3% p=0.003	differences between the
Stop Dates	n = 95 did not meet	-The staff applied	Significant difference between		intervention and control groups,
5/2000 - 12/2002	inclusion criteria	comprehensive geriatric	groups for each day (1-7)	p =0.001	there was still a strong
	n= 11 Refused to	assessment, management	Delirious after the seventh		association between number of
Purpose	participate	and rehabilitation	postoperative day	18% vs. 52% p< 0.001	days with postoperative delirium
To determine whether a	n=27 missing due to		Delirious at discharge	0 vs. 20 patients p < 0.001	and being treated in the control
postoperative multi-	failed inclusion routines	Main content of intervention	-		group.
factorial intervention	n = 21 suffered fracture	protocol	Secondary outcomes	Intervention vs. Control	
program, including	in hospital	-Staff education	Urinary infections	39.3% vs. 60.3% p =0.018	The effect of the intervention
comprehensive geriatric	-severe rheumatoid	-Teamwork	Sleeping problems	28.6% vs. 50.7% p = 0.011	program seemed to reduce the
assessment,	arthritis	-Individual care planning	Falls	17.9% vs. 34.3% p = 0.034	incidence of delirium on the first
management and	-severe hip	-Delirium prevention,	Decubitus ulcers	10.7% vs. 23.6% p=0.059	postoperative day.
rehabilitation, can	osteoarthritis	detection, treatment	Assessments of underlying		
reduce delirium and	-severe renal failure	-Prevention/treatment of	causes of delirium		This may be explained by the
improve outcome in	-pathological fracture	complications	documented in		fact that, when the patients
patients with femoral	-patients who were	-infection	medical records	2.28(1.25) vs. 0.90(0.90) p<.001	arrived at the intervention ward,
neck fractures.	bedridden before	-anemia	Length of Stay (LOS) (days)	28(17.9) vs. 38(40.6) p= 0.028	they were immediately and
	fracture due to the	-embolism	LOS for patients with postop		systematically assessed to
Funding source(s):	operation methods that	-Bowel/bladder function	delirium	31.4(19.3) vs. 43.6 (42.7) p= 0.032	detect, treat and prevent any
Vardal Foundation, Joint	were planned to be		LOS for delirium patients with		complications that would cause
Committee of the	used in the study		dementia	3.2 (4.1) vs 12.8 (17.6), p = 0.003	delirium.
Northern Health Region			Dementia patients with postop		
of Sweden , JC Kempe			delirium at discharge	0 vs 15, p <0.001	Patients with dementia seemed
Memorial Foundation,	Other assessments				to have benefited from the
Foundation of the	Geriatric Depression	n = 97 control	Delirium assessment:	See above	intervention program.
Medical Faculty,	Scale (GDS)		Baseline characteristics	See above	
University of Umeå,	Prefracture Personal	Men and women (76.28%)	Primary outcomes	See above	All parts of the intervention
County Council of	ADLs (P-ADL)	Mean age 82 (5.6)	Secondary outcomes	See above	program, which are probably
Västerbotten and					equally important should be
Swedish Research		Protocol	Delirious control patients		systematically adapted with
Council, Grant		Usual postoperative care in	received		focus of detection, prevention
		the orthopedic department	More sedatives	41.7% <i>vs</i> 15.4%, p=0.008	and treatment of delirium
Quality Score:			More opioid drugs on demand	61.7% <i>v</i> s 30.8%, <i>p</i> =0.004	
6		Patients needing further in-			Limitation
		hospital rehabilitation (n = 40)			-psychiatric symptoms and
Risk of Bias:		admitted to a geriatric ward			cognitive testing only 1 time
High		but not the intervention ward			during hospitalization

**Conclusion**: This study shows that postoperative delirium can be successfully treated by a team applying comprehensive geriatric assessment, management and rehabilitation. The intervention program resulted in fewer days with delirium, fewer other complications, and shorter hospital stays. Implementing this intervention program will probably have a great humanitarian and economic impact, and is probably applicable to surgery on old people in general. Therefore, the organization of surgical wards should be reconsidered and adapted to the needs of the oldest and frailest patients.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Significant differences in baseline characteristics
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	No blinding during outcome assessment (record reviews)
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

# G-3 Chen CC, Lin MT, Tien YW, et al. Modified hospital elder life program: effects on abdominal surgery patients. J Am Coll Surg. 2011;213(2):245-52.

				Results		
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments	
	N = 217 eligible patients	n = 102 HELP intervention	Delirium assessment:	2 trained/blinded study assistants	10 patients lost to attrition	
Taiwan	N = 28 declined		CAM	conducted assessments at admission	were not included in	
	participation	(enrolled May 2008 to April 2009)	MMSE	and hospital discharge; inter-rater	analysis	
Setting	n = 6 "not feeling well"			reliability and severity not discussed		
Gastrointestinal ward	n = 4 family members	Mean Age 73.3( 5.4)				
of an urban medical	declined	Men and women (46.1%)	Baseline characteristics	Significant difference	The modified HELP	
center	n = 18 did not consent			Intervention vs. control	intervention has great	
		Modified HELP Protocol	More periampullary cancer	29.4% vs 15.6% (p = 0.03).	potential to be clinically	
Study Design	N = 189 enrolled	Implemented by full-time trained HELP	More Whipple procedures		feasible for effectively	
Pre/post comparison;	N = 10 not in analysis	nurse blinded to the study outcomes,	performed	18.6% vs 9.1% (p = 0.05)	reducing in-hospital	
clinical trial	n = 7 died	who was not an outcomes assessor.	Longer surgery duration	226.8 ± 91.1 minutes vs 199.0 ± 68.7	functional decline among	
	n = 3 withdrew consent			minutes ( $p = 0.04$ ),	older surgical patients.	
Selection method:		The same attending physicians	Fewer open procedures	73% vs 88.3% , p = 0.01	elder eurgieur patiente.	
Consecutive patients	Comparison groups	provided clinical care to both groups	Better ADL performance	98.0(6.1) vs. 92.2 (13.6) (p < 0.001)	Receiving 7 days of the	
who underwent	N = 179	provided elimital care to beth groups	Better nutritional status	24.0(3.5) vs. 20.7(4.0) (p < 0.001)	modified HELP	
elective abdominal	n = 102 intervention	Daily hospital-based care including 3	Detter Huthtonial status	24.0(0.0) V3. 20.7(4.0) (p < 0.001)	intervention prevented full	
	n = 77 control	key protocols:			functional loss in 2 to 3	
surgery procedures;		1) early mobilization	Drimony outcomes	Intervention vs. control	ADLs (or partial loss in	
allocation by date of	Inclusion	-ambulation or active range-of-motion	Primary outcomes			
admission	Inclusion		Incidence of delirium	0 (0%) vs 12 (16%), p <0.001	function across more	
	Age ≥ 65	exercise 3 times daily			ADLs), decreased weight	
Study Length/Start-	-Admitted to	2) nutritional assistance	Change from baseline to		loss by 30%, and reduced	
Stop Dates	gastrointestinal ward	-daily oral care involving tooth	discharge		delirium rates before	
8/2007-4/2009	-Scheduled for elective	brushing, nutrition screening, diet	Better functional status		hospital discharge, which	
	abdominal surgery	education, and feeding assistance if	BI Score decline	11.8 vs. 27.9 points; p < 0.001	are clinically important	
Purpose	-Expected LOS longer	needed	Better nutritional status		results.	
To examine the	than 6 days	<ol><li>therapeutic (cognitive) activities</li></ol>	MNA score decline	2.8 vs 7.6 points; (p < 0.001)		
effects of a modified		-orientating communication and	Better cognitive function			
Hospital Elder Life	Exclusion	cognitively stimulating activities, such	MMSE score decline	0.4 vs 1.4 MMSE points	Family caregivers are also	
Program (HELP)	N =34	as discussing current events or word			present at bedside in	
intervention in	n = 9 with profound	games 3 times daily)	Secondary outcomes		Taiwan which may have	
reducing functional	sensory impairment or		Fewer depressive symptoms		helped the nurse who was	
decline of older	aphasia that precluded	All 3 protocols implemented as soon	(decline of GDS-15)	0.3 vs. 4.4 p<0.001	administering HELP	
patients during	verbal communication	as patents returned to surgical inpatient	Reduced body weight		interventions	
hospitalization for	n = 14 Intubation or	ward and ended at hospital discharge	Less decline in kg	2.2 vs. 3.1 p=0.002		
abdominal surgery.	respiratory isolation		Grip strength			
	n = 8 Severe dementia,	54% of intervention group received	Less decline in kg	1.2 vs. 2.6 p<0.001	Limitations	
Funding source(s):	coma, critical condition	approximately 7 days of the modified	Ũ		-possible selection bias	
-Taiwan National		HELP protocol			-temporal separation of	
Science Council grant	Outcome assessment	•			study groups (study	
-Retirement Research	tools	n = 77 control group (usual care)	Delirium assessment	See above	design)	
Foundation grant	Chinese BI (functional				-intervention tested on	
-Career development	status)	(admitted 8/2007-4/2008)	Baseline characteristics	See above	only one ward	
grant from the	Chinese Mini-Nutritional	(			-other confounding	
National Health	Assessment (MNA)	Mean Age 72.6 (6.1)	Primary and secondary	See above	factors possible	
Research Institute	Chinese Geriatric	Men and women (44.2%)	outcomes			
	Depression Scale Short					
Quality Score	Form (GDS-15)					
4						
Risk of Bias:						
Risk of Bias: High						

Conclusion: The modified HELP intervention was successfully implemented and it ameliorated postsurgical functional decline and delirium rates for older patients undergoing common elective, abdominal surgical procedures.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant baseline differences between groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – allocation by date of admission
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Only outcome assessors blinded
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	(dropouts 5%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Study design (pre/post) Baseline imbalances Possibility of confounding factors such as increased medical attention from trained nurse in HELP
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score • from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on <u>the criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains •

  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains 0

G3-Inouye SK, Bogardus ST, Jr., Williams CS, et al. The role of adherence on the effectiveness of nonpharmacologic interventions: evidence from the delirium prevention trial. Arch Intern Med. 2003;163(8):958-64.

Study	Population	Intervention	Results	i	Adverse Effects/	
Characteristics			Measure	Outcome	Comments	
nouye 2003	N = 871 met inclusion	N = 422	Delirium assessment:	MMSE, CAM measured at	No adverse events associated	
JSA	criteria		MMSE	baseline within 48 hrs of	with protocols	
	n = 422 final study	Protocol	CAM	admission, and daily by		
etting	sample	-implemented by Elder Life		separate blind research team		
ledicine service at a		Specialists (trained hospital		members who underwent	Most common reasons for	
niversity hospital	Men and women (60.9%)	staff members) and assisted		standardization, and inter-rater	non-adherence in13% of	
	Mean age 79.7 (6.11)	by trained volunteers,		reliability assessment	patient days	
Study Design	MMSE = 23.7(4.57)	by trained volunteers,			-52% lack of availability of	
Prospective	MMSE <24 = 41%	-overseen by a geriatric	Baseline characteristics	86.7% with impairment of IADLs	intervention staff members	
bservational	Modified Blessed DRS	clinical nurse specialist and	Dasenne characteristics	34.4% impairment of ADLs	-27% patient refusal	
DServational						
	1.6(2.17)	geriatrician		High indexes of illness burden	-10% lack of availability of	
Selection method	Baseline delirium risk			-mean APACHE II 15.5	patient because of medical	
Consecutive patients	Intermediate 72%	-all patients assigned to		-mean Charlson index 3.1	procedures	
admitted to one	High 28%	receive orientation, mobility,	Primary outcomes		-7% severe medical	
general medicine floor		and therapeutic activities	Overall rate of complete adherence with		symptoms preventing	
	Inclusion	protocol,	all intervention protocols	57%	participation or medical	
Study Length/Start-	Age ≥ 70		Combined partial and complete		contraindication	
Stop Dates	-no delirium at admission	-other protocols were	adherence	87%		
3/1995-3/1998	-at least intermediate risk	assigned according to risk				
	of delirium at baseline	factors present at screening.	Adherence rate by intervention protocol		Multivariable analysis	
Purpose		iactore process at corecimig.	across all patient-days		Unadjusted model indicated	
To examine the impact	Exclusion	-other protocols include	Orientation	86%	substantial reduction risk of	
of level of adherence	N = 335	sleep, hearing or vision, and	Mobility	36%	delirium associated with eac	
on effectiveness of the	n=117 inability to	volume repletion		63%		
		volume repletion	Therapeutic activities		1-point increase in adherenc	
ntervention strategy in	participate in interviews		Sleep	10%	score	
a large clinical trial of	for reasons such as	- patients were reassessed	Vision-hearing	83%		
nonpharmacologic	profound aphasia or	daily for changes in risk	Volume repletion	57%	Adjusted model controlled for	
nterventions to	intubation	factors that might necessitate			age, sex, education, Charlson	
prevent delirium	n=34 coma or terminal	changes in their protocol	Adherence Group	Delirium Rates by Protocol	score, depression, impairmer	
	illness	assignments		Orientation/Mobility/Therapeutic	in ADLs, illness severity,	
Funding source(s):	n=89 hospital stay of less		Low	24% / 14% / 12%	MMSE, blood urea nitrogen-	
Grant from NIA and in-	than 48 hours	-staff and volunteers	Intermediate	13% / 10% / 10%	creatinine ration, and visual	
kind support from	n=95 unavailability of	underwent quarterly	High	7% / 3% / 4%	impairment	
Claude D. Pepper	interviewer or patient	standardization with	p-value	<0.001 / .01 /.06		
Older Americans		completion of competency-			In the fully adjusted model, th	
Independence Center	n=114 refusals by	based checklists for	Significant decrease in incidence of		risk of delirium of a patient in	
given by the NIA	patients, families, or	consistency	delirium with higher levels of adherence		the highest adherence group	
	physicians	conclosed	using composite adherence score		was 89% lower than the risk	
	physiolaris	-level of adherence recorded	(orientation, mobility, and therapeutic		the lowest adherence group.	
Quality Score:	Excluded patients did not	daily as full or partial	activities).	p <sub>trend</sub> = .002	the lowest autorence group.	
Suality Score.	differ significantly from	daily as full of partial	activities).	Ptrend = .002	In the highest adherence	
J			Stratified by baseling deliving			
Diak of Diag	enrolled patients in terms		Stratified by baseline delirium		group, the rate of delirium wa	
Risk of Bias:	of age, sex, or baseline		risk group (intermediate vs.		less than 3%.	
Jnclear	delirium risk		high), the relationship of lower			
			incidence of delirium with			
			higher levels of adherence	P <sub>trend</sub> =.04 for each delirium		
			persisted	group		
			Protective Effect of Adherence on			
			Delirium Rate			
			Unadjusted Adherence	OR .67(.5483) p<0.001		
			Full adjusted adherence	OR .69 (0.56-0.87) p= 0.001		
			1		1	

of delirium in a direct graded fashion, with extremely low levels of delirium in the highest adherence group. Thus, adherence must be ensured in nonpharmacologic interventions to optimize 24 effectiveness.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	Unclear	Single group observational study, but multivariable analysis did not reveal confounding variables; no difference between included/ excluded subjects
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	Unclear	Participants may have been aware of the interventions/protocols they received
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):	1		BIAS RATING = Unclear
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low ri ٠

  - High risk of bias: High risk of bias on 2 or more of 6 domains

G3-G5-Lundstrom M, Edlund A, Karlsson S, et al. A multifactorial intervention program reduces the duration of delirium, length of hospitalization, and mortality in delirious patients. J Am Geriatr Soc. 2005;53(4):622-8.

O fair all a	Denviation	Internetien Orecord		Results	0.000
Study	Population	Intervention Groups	Measure	Outcome	Comments Conclusion
Characteristics	N - 400		Delinium eccentrati	Thursda fithe and the second of ODO and a second	
Lundstrom M 2005	N = 400	n = 200 Intervention group	Delirium assessment:	Three of the authors rate OBS scale and	Too few patients had
Sweden			DSM-IV	MMSE on days 1,3, and 7, then determined	dementia in the present study
	Inclusion	Men /women% 39.0/61.0		delirium according to DSM-IV criteria (90%	to allow analyses of patients
Setting	Age ≥70	Mean age 79.4 (5.6)		inter-rater agreement) (authors blinded to	with dementia separately, but
Department of	Informed consent			allocation)	no patient with dementia
General Internal		1. A 2-day course for staff on			remained delirious on Day 7 in
Medicine, University	Exclusion	geriatric medicine focusing on	Baseline characteristics	Significant difference between groups	the intervention ward,
Hospital	N = not described	assessment, prevention, and		Intervention vs control	compared with four patients
	Age <70	treatment of delirium	Age	79,4 (5.6) vs 80,7 (6.2), p=.02	still delirious on Day 7 in the
Study Design	Declined participation		Male% vs Female %	39.0%/ 61.0% vs 49.5%/50.5%, p=.04	control ward, which might
Prospective		2. Education concerning caregiver-	Diabetes mellitus	42.5% vs 23.5% p<0.001	indicate that delirium in
Controlled clinical trial	Other assessment (all	patient interaction focusing on	Stroke %	170% vs 25.0%, p=05	patients with dementia can be
	patients):	patients with dementia and		10% vs 25.0%, p=.03	successfully treated.
		•	Myocardial infarction	10% vs 4.5%, p=.05	successivily treated.
Selection method	RA assessed on Days 1,	delirium			
Consecutive	3, and 7 after admission		Logistic Regression to	Delirious Patients in the Two Wards	
dmission to 2 wards	Organic Brain Syndrome	<ol><li>Reorganization from a task-</li></ol>	Control for Baseline	(N=125; n = 63 vs n = 62))	Limitations
ntervention ward;	(OBS) Scale,	allocation care system to a patient-	Differences		-randomization/allocation
ontrol ward)	MMSE	allocation system with	Ward	OR=3.12 (1.43–6.81)	dependent on bed availability
Random allocation	Katz ADL index	individualized care	Stroke on admission	OR=1.44 (0.62–3.35)	-RA assessors not blinded
om ED based on	Vision testing		Sex	OR=1.35 (0.59-3.05)	-assessments not done daily
vailable bed;	(admission)	4. Guidance for nursing staff once	Age	OR=1.01 (0.95–1.08)	-discharged patients
eadmissions within 3	Hearing testing	a month	Diabetes mellitus	OR=0.53 (0.22-1.27)	regarded as not delirious on
nonths of discharge	(admission)				Day 7 (1 patient assessed as
admitted to the same	(ddfflooloff)	No blinding	Primary outcomes	Day 1 vs Day 3	delirious within 24 h of
vard as previous		No binding	Delirium incidence	123/400 (30.8%) vs 82/400 (20.5%),p <.001	discharge)
-			Deminum incluence		uischarge)
reatment			Delivium may aleres (24b)	Intervention vs control	
			Delirium prevalence (24h)	31.5% vs 31.0%; p=.91	
Study Length/Start-			Delirium incidence (Day3)	58.7% vs 72.6%; p=.10	
Stop Dates			Delirium incidence (Day7)	30.2% vs 59.7%; p=.001	Conclusion
lot described					
			Secondary outcomes	Intervention vs control	This study shows that a
Purpose			Length of stay( days)	9.4 (8.2) vs 13.4 (2.3); p<.001	multifactorial intervention
o investigate			Return to home/apt	86.6% vs 82.4%; p=.29	program reduces the duration
vhether an education					of delirium, length of hospital
program and a			Delirious patients		stay, and mortality in delirious
eorganization of			Return to home/apt	78.3% vs 60%; p=.05	patients.
ursing and medical			Mortality	2 (3.2%) vs9 (14.5%); p=.03	
are improved the			wortditty	2 (0.2 /0) 000 (17.0 /0), p=.00	
outcome for older		n = 200 Control group	Delirium assessment:		
elirious patients.		n – 200 Control group	Demnum assessment.		
ennous patients.		Mankungan % 40 E/E0 E		Cas shave	
unding course(a)		Men/women % 49.5/50.5	Deseline	See above	
unding source(s):		Mean age 80.7 (6.2)	Baseline		
oint Committee of			characteristics/measures		
heNorthern Health		Usual hospital care organized in a			
Region of Sweden		task-allocation care system;			
Visare Norr), et al		-the same caregiver handled	Primary outcomes		
		particular tasks for all patients,	-		
uality Score		-no clinical caregiver had full	Secondary outcomes		
-		responsibility for an individual	· · · · <b>,</b> · · · · · · · · · · · · · · · · · · ·		
		patient during his or her entire			
Risk of Bias:		hospitalization.			
High					
iigii		Staff aware that a corponing of			
		Staff aware that a screening of			
		delirium prevalence was being			
	1	performed			26

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Randomization based on bed availability; significant baseline differences between groups
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Allocation concealed only for authors who determined delirium dx
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	No blinding except authors who determined delirium dx
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	No information on number of patients excluded
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Numerous baseline imbalances, but analyzed to determine OR related to delirious patients Unknown confounders possible because delirium assessment not done daily
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		<b>v</b>
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-G5-Tabet N, Hudson S, Sweeney V, Sauer J, Bryant C, Macdonald A, et al. An educational intervention can prevent delirium on acute medical wards. Age Ageing. 2005;34(2):152-6.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Tabet N 2005	N = 250 recruited	n = 122 intervention ward	Delirium assessment:	Unblinded research old age	
UK	n = 122 intervention	n = 6 patient case notes not	Delirium Rating Scale (DRS)	psychiatrists carried out assessments	Key Points:
	n = 128 control	located	Abbreviated Mental Test Score	during the daytime. Inter-rater	,
Setting			(AMTS)	reliability not discussed	1. Delirium is a commor
Acute admissions wards	Inclusion	Men and/women (53.28%)	(*******)	· · · · · · · · · · · · · · · · · · ·	disorder among
n inner-city teaching	All admissions to intervention/	Mean age 81.39	Baseline characteristics	Significant difference between groups	hospitalized older peopl
hospital	control wards eligible			Intervention vs control	
	Age ≥70	Educational Package	Mean age	81.39 vs 79.28, p = 0.007	Established cases are
Study Design	Understood and spoke	1) A 1-hour session including a			not readily improved by
single-blind case control	English	formal presentation and small	Primary outcomes	Significant difference between groups	intervention.
study	Agreed to participate	group discussion	point prevalence of delirium	12/122 (9.8%) vs 25/128 (19,.5%)	
, <b>,</b>	No recorded symptoms of	5		p=0.034	2. Increasing doctors'
Selection method	delirium in medical or nursing	2) Written information and			and nurses' awareness
Admissions to 2 general	notes on admission	gidelines on ghow to prevent,	Recognition of delirium cases	8/12 (66.66%) vs 6/23 (26.09%),	of delirium can be
acute medical units with	In hospital >24 h	recognize and manage delirium	5	p=0.001	achieved through a brie
similar internal physical	Informed consent	in older people			ad inexpensive
eatures, separate nursing					educational program.
and medical teams on the	Exclusion	3) Regular one-to-one and small			1 0
ame hospital floor.	N = not described	group discussions lasting up to			3. The educational
Admissions based on bed	Patients who did not meet	an hour during with staff were			program significantly
availability.	inclusion criteria	encouraged to discuss			decreases the
,		discharged challenging cases			prevalence of delirium
Study Length/Start-Stop	Components of education	they had encountered with the			among older inpatients
Dates	package	aim of enhancing their learning			and increases
12/2001 to 8/2002	General information on	experience with specific			recognition of cases.
	delirium	examples			J J
Purpose	-definition				4. Such an educational
To test whether an	-etiology	Ward staff received no			program can be easily
educational package on	-epidemiology	incentives for adopting the			rolled out across hospit
he recognition and	-symptoms	intervention			unity caring for older
nanagement of delirium	-outcomes				people.
delivered to medical and	Prevention	n = 128 control ward	Delirium assessment:	See above	
nursing staff would	<ul> <li>-risk factor recognition</li> </ul>				
lecrease the point	-active management of	Men and women (51.56%	Baseline characteristics	See above	
prevalence of delirium	treatable risk factors	Mean age 79.28			
among older hospitalized	-high vigilance		Primary outcomes	See above	
patients	-active early intervention	Usual care			
	Management	No educational package			
Funding source(s):	-environmental	Established practice was			
Not described (conflict of	-nursing care	maintained throughout			
nterest statements =	-investigations				
none")	-identifying and treating				
	underlying causes				
Quality Score	-management of symptoms				
1	Non-pharmacological				
	treatment				
Risk of Bias:	-assess after 48 h				
High	-discontinue before				
	discharge				
					1

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant difference in mean age between groups
• Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Psychiatrists not blind to study group
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Outcome assessors not blind to study group
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Not described detail s of exclusion Not reported SD
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Baseline imbalance (age) Limited baseline data reported so possible presence of confounding variables Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-Robinson S, Rich C, Weitzel T, et al. Delirium prevention for cognitive, sensory, and mobility impairments. Res Theory Nurs Pract. 2008;22(2):103-13.

<b>e</b> ( )	<b>_</b>		F F		
Study Characteristics	Population	Study Groups	Measure	Outcome	Comments
Robinson 2008	N = 160	n = 80 post intervention (admitted to	Delirium assessment:	Chart review of medical records to	
USA	n = 80 matched pairs	the renal unit after implementation	Use of CAM and other data	extract data; investigators	Eleven of the 80
		of the protocol)	extracted using the Chart-	determined the chart based method	participants in the post
Setting	Matching criteria	. ,	Based Method for the	was suitable for evaluating broad	intervention group became
Jniversity Hospital,	-age (w/in 5 years),	Men and women (54%)	Identification of Delirium	based clinical programs but not for	delirious, despite
renal unit	-gender, -presence of dementia	Mean age 78.82		diagnostic purposes in patient care	implementation of the protocol.
Study Design	-vision impairment	Protocol	Baseline characteristics	No significant differences between	
Matched Pre/post	-hearing impairment	-On admission, patients assessed for		groups in baseline characteristics or	Nursing staff continued to
design	-mobility impairment	risk factors by the registered nurse admitting the patient.		risk factors	use the protocol for these patients to minimize the
Selection method	Inclusion		Risk factors present	All patients (each group, n)	effects of the delirium.
Convenience sample	Age > 65	-If patient had any of the risk factors,	1 risk factor	39	
of patients admitted	-any combination of	appropriate interventions were	2 risk factors	28	Many of these patients
before and after	delirium risk factors	implemented to avoid delirium.	3 risk factors	11	suffered from renal failure.
implementation of the	-dementia		4 risk factors	2	Fluid and electrolyte
protocols	- vision impairment,	-Interventions	Dementia	12 (15%)	disturbances were commo
510106013	-hearing impairment	-implemented by trained nursing	Vision impaired	34 (42.5%)	and may have contributed
Study Length/Start-	0 1	assistants	Hearing impaired	29 (36.3%)	to the delirium.
	- mobility impairment	-Hospital Elder Life Program (HELP)	0 1		to the delinum.
Stop Dates	Admission prior to and		Mobility impaired	58 (72.5%)	
Not discussed	after implementation of the	protocols			Limitations
_	delirium prevention	-Geriatric Nursing Protocols for Best	<b>.</b>		-identification of delirium
Purpose	protocol	Practice (Forman, Mion et al 2003)	Primary outcomes	Pre n (%) vs. Post n (%)	via chart review
To determine if a		-implementation of Delirium	Demonstrated symptoms of		-CAM was not consistent
delirium prevention	Exclusion	Prevention Measures by Risk Factor	delirium at admission	(30) 37.5% vs. (11)13.8% p < .001	used pre or post
protocol targeting the	Not discussed	(Table 1 in PDF)			intervention
risk factors could			Developed delirium on hospital		-other risk factor
prevent delirium in	Data source	<ul> <li>Clinical nurse III or nurse manager</li> </ul>	day 2	28 (93%) vs. (9) 82%	identification were not
older adults	Medical records	monitored implementation of protocols			formally assessed using
hospitalized on a	Instrument = Chart Based	daily	Patients with dementia and		recognized instruments
renal unit.	Method for the		other risk factors	N = 12 (all patients)	-the relationship of the
	Identification of Delirium	Nursing Assistant Training	Developed delirium (n)	Pre vs post	prevention protocol to each
Funding source(s):		-4 half day classes		6 vs 1	risk factor could not be
Not discussed		-delirium			examined
		-dementia			-the nurses monitoring the
Quality Score:		-sensory losses			protocol implementation di
3		-mobility			not record the number of
-		Nursing staff also trained during staff			times the protocol was not
Risk of Bias:		meetings			implemented
High					-data on duration of
i iigii		n = 80 pre intervention (control)	Delirium assessment:	See above	delirium and the presence
		n = ov pre intervention (control)			of delirium at discharge
		Men and women (54%)	Baseline characteristics	See above	were not recorded
		Mean age 79.18	<b>_</b> .		
			Primary outcomes	See above	
		Protocol			
	1	Usual care	1		1

**Conclusion**: The findings of this study indicate that simple interventions targeting dementia, vision loss, hearing loss, and mobility limitations can prevent delirium in some patients when these risk factors are identified and targeted by nurses. Although the protocol prevented some cases of delirium, nursing protocols will not prevent delirium in all elderly patients. A significant reduction in delirium, from 37.5% before protocol implementation to 13.8% after implementation, occurred in the elders receiving the protocol.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
1. Balanced allocation (1 point if achieved):         O Description of the method used for balanced allocation in sufficient detail to allow an         assessment of whether it should produce comparable groups. This will typically include         either a valid randomization procedure or prospective individual matching between         intervention and control groups.         Evidence that balance was achieved	1	Low	Matched pairs
<ol> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ol>	0	High	NA – Pre/post design
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA – Pre/post design
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	High	Due to study design, there was insufficient data to report on important outcomes (see limitations)
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Pre/post design; historical cohorts Risk factors were not assessed with valid instruments Likely that confounders were present and not controlled (even in the presence of matching the cohorts) Funding not described
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	0		Chart review did not include consistent validated assessment
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G5-Heymann A, Radtke F, Schiemann A, et al. Delayed treatment of delirium increases mortality rate in intensive care unit patients. J Int Med Res. 2010;38(5):1584-95.

Study Characteristics	Population	Study Groups	Measure	Outcome	Comments
Heymann A 2010	N = 2640 patients	n = 184 immediate therapy	Delirium assessment:	Administered on 3 consecutive days	Important results
Germany	screened	(initiated within 24 h after	DDS	(includes severity; inter-rater reliability not	-a delay in starting
-	n = 2222 excluded	delirium dx)		discussed)	delirium therapy was
Setting	N = 418 patients analyzed				associated with an
Jniversity Hospital	n = 214 DDS <7	Men and women (33%)	Baseline characteristics	Significant difference between groups	elevated mortality risk
CU	N = 204 DDS ≥7	Mean age 62.5 (18-95)		Delirium (204) vs No Delirium (214)	-all ICU scores
	n = 184 immediate therapy	APACHE II score 20.2 (5-38)	Admission APACHE II	p <0.001 (detail not provided)	decreased significantly
Study Design	n = 20 delayed therapy	SOFA score 5.7 (0-14)	Admission SOFA	p <0.001 (detail not provided)	during the course of th
Prospective		TISS-28 score 33.3 (11-62)	Admission TISS-28	p <0.001 (detail not provided)	ICU stay in the
observational	All patients delirium	100-20 30010 33.3 (11-02)	Admission 1133-20	All delirium patients N = 204	immediate therapy gro
Doservational	incidence	Therapy protocol	Gender	Male 66.2% vs Female 33.8%, $p = 0.001$	but not in the delayed
Selection method	48.8%	Level of sedation evaluated	Gender	Immediate (184) vs delayed (20)	5
	40.0%		Admission ADACHE II		therapy group
Consecutive		every 8 h (RASS)	Admission APACHE II	20.2 (5-38) vs 24.7 (18-36), p = 0.005	-this finding supports
admissions to ICU	All delirium patients:	RASS ≥ -2: DDS			the idea that a delay in
neeting inclusion	Median age 63 (18-95)	administered	Primary outcomes (delirium)	Significant difference between groups	therapy for delirium lea
criteria	Men and women (33.85)	DDS administered 3		Immediate (184) vs delayed (20)	to aggravation of illnes
		consecutive days	Recurrent delirium episodes	2.2 (1.6) vs 2.9 (1.7), p = 0.036	and that delirium is not
Study Length/Start-	Inclusion	DDS >7 = delirium	Severity at delirium dx	13.9 (5.6) vs 10.2 (3.3), p = 0.001	improved when delaye
Stop Dates	Age ≥18	Standard delirium treatment	Reduction in DDS	Greater in immediate (p = 0.004) detail not	treatment starts.
3/2006 – 11/2006	Admission to ICU	protocol initiated		provided	-although the DSS init
2/2007 – 5/2007	-postoperative	<ul> <li>-medications administered</li> </ul>	Correlation time of theray onset		score was lower in the
	-postoperative	according to protocol	with rate of DDS reduction	p = 0.014 (See Figure 2)	delayed therapy group
Purpose	complications		Hypoactive delirium	14% vs 40%, p = 0.041	the immediate therapy
To clarify the effect of	-respiratory failure		DDS on last day in ICU for	Last day vs first day	group had better deliriu
a delay in receiving	ICU LOS >72 hours		immediate therapy group	5.5 (5.7) vs 13.9 (5.6), p <0.001	and other outcomes
delirium-specific	Informed consent		DDS on last day in ICU for delayed		
herapy on patients			therapy group	7.3 (4,9) vs 10.2 (3.3), NS	Limitations
outcome.	Exclusion		1,50 1		-the number of patien
	N = 2222		Other clinical outcomes	Significant difference between groups	analyzed in each group
Funding source(s):	n = 27 age <18			Immediate (184) vs delayed (20)	was small
Not described	n = 1934 LOS <72 hours		Mortality	16 (8.7%) vs 7 (35%), p = 0.003	-DDS cutoff of 7
	n = no evaluation possible or		Risk	HR 3.023 (1.056-8.656)	probably did not detect
	missing values		Significant for age	HR 1.035 (1.002-1.070), p = 0.038	all types of delirium (du
Quality Score	n = 214 DDS <7		Nosocomial infections	134 (72.8%) vs 19 (95.0%), p = 0.029	to low sensitivity of DD
2	Moribund		Pneumonia	92 (50%) vs 16 (80.0%), p = 0.017	score)
-	Coma		l nounona	HR 1.850 (1.023-3.343), $p = 0.042$	-fewer patients in the
Risk of Bias:	Severe neurological		APACHE II at discharge	16.9 (6-43) vs 24.1 (7-45), p = 0.002	delayed therapy group
High	impairment (brain injury)		SOFA score at discharge	3.9 (0-18)  vs  7.5 (1-19),  p = 0.005	received neuroleptic
light	inipairment (brain injury)		TISS-28 score at discharge	27.3 (3-66)  vs  36.9 (13060)  p = 0.001	treatment (35% vs 78%
	Assessment tools		1133-28 score at discharge	27.3(3-00) vs $30.9(13000)$ p = 0.001	p not included) which
	Richmond Agitation		No significant difference between	Mechanical ventilation days	may have influence
	Sedation Scale (RASS)		0		outcomess
	Delirium Detection Score	n = 20 delayed therapy	groups Delirium assessment:	ICU LOS See above	outcomess
	(DDS)	(initiated >24 h after			
Chroni (APAC Simplif Assess Therap	Acute Physiologic and Chronic Health Evaluation II	delirium dx)	Baseline characteristics	See above	
	(APACHE II)	Men and women (45%%)	Primary outcomes	See above	
	Simplified Organ Failure	Mean age 69.4 (42-90)	Secondamy auto-mas	See above	
	Assessment (SOFA)	APACHE II score 24.7 (18-	Secondary outcomes	See above	
	Therapeutic Intervention	36)			
	Scoring System (TISS-28)	SOFA score 7.1 (3-18)			
		TISS-28 score 36.7 (19-57)			
		Therapy protocol (as above)			

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
Balanced allocation (1 point if achieved):         Description of the method used for balanced allocation in sufficient detail to allow an         assessment of whether it should produce comparable groups. This will typically include         either a valid randomization procedure or prospective individual matching between         intervention and control groups.	0	High	Many significant differences between all patients and/or study groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA – observational study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	High	Detailed information not provided for some outcomes; authors note difference in use of neuroleptics may have influenced outcomes (not analyzed)
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Significant baseline imbalances Possibility of confounders (neuroleptic use or study group imbalances) Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Delayed n <50
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 2

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G3-G5-Milisen K, Foreman MD, Abraham IL, et al. A nurse-led interdisciplinary intervention program for delirium in elderly hip-fracture patients. J Am Geriatr Soc. 2001;49(5):523-32.

				Results	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Milisen K 2001	N = 120 patients	n = 60 intervention cohort	Delirium assessment:	Trained research nurses obtained	There was neither a statistical
Belgium	analyzed	(9/1997 – 3/1998)	CAM	information about cognitive functioning	nor clinical effect for the
1	n = 60 pre-intervention		MMSE	(CAM and MMSE) on the first, third, fifth,	intervention relative to functional
Setting	n = 60 post-intervention	Men and women (81.7%)		eighth, and twelfth postoperative days.	status.
Urban academic		Median age 82 (13)			
medical center	Inclusion		Baseline characteristics	Significant differences :	There was no significant
1	<ul> <li>Patients admitted to the</li> </ul>	Overview		Intervention vs. Control	difference in functional status
Study Design	ER w/ traumatic fracture of	<ul> <li>A system of enhanced</li> </ul>	Cardiac comorbidity	13.3% vs. 30% p=.045	between the intervention and
Prospective	proximal femur (intra-and	quality of nursing care for	Vascular comorbidity	5% vs. 25% p=.004	control cohorts or for either the
longitudinal (pre/post	extracapsular)	older hip- fracture patients	Abdominal comorbidity	5% vs. 20% p=.025	delirious or nondelirious patients.
design)	<ul> <li>Hospitalized in one of two</li> </ul>	was developed,			
	traumatological nursing	implemented, and tested.	Primary outcomes	Intervention vs. Control	However delirious patients in
Selection method	units w/in 24 h of surgery	-Nurses identified high-risk	Incidence of delirium, n%	12 (20.0%) vs 14 (23.3%) (p = 0.82 – NS)	both cohorts were more
Patients admitted to	<ul> <li>Spoke Dutch and verbally</li> </ul>	patients and provided			dependent after discharge and 3
ER with traumatic	testable	prompt anti-delirium	Duration of delirium (days)	1 (1) vs. 4 (5.5), p=.03	months after discharge.
fracture of proximal		interventions to reduce and			
femur	Exclusion	treat delirium.	Severity of delirium		Neither cohort of the delirious
1	-Multiple trauma	<ul> <li>Access to readily available</li> </ul>	Mean total CAM scores	Delirium vs no delirium	patients regained their pre-
Study Length/Start-	concussion of the brain	consultants and were able to	Intervention group range	3.82 (2.8) to 1.91 (2.3) vs 0.98 (1.6) to 0.87	fracture functional status.
Stop Dates	-Pathological fractures,	administer regularly		(1.7)	
9/1996 - 3/1997	surgery occurring more	scheduled pain medications.	Control group range	6.92 (2.8) to 5.0 (3,.1) vs 1.35 (2,.3) to 0.76	Delirious patients in both cohorts
9/1997 - 3/1998	than 72 hours after		<b>.</b>	(1.4)	also had a slower functional
1	admission, aphasia, -	Protocol components	Linear mixed model analysis	$\dot{p} = 0.0152$ , intervention vs control	rehabilitation over time.
Purpose	blindness	1. Education of nursing staff	,	No significant difference in change over time	
To develop and test	-Deafness	2. Systematic cognitive		5	There was no significant
the effect of a nurse-	-Fewer than 9 years of	screening		Significant difference in decrease in CAM	difference in length of stay
led interdisciplinary	formal education	3. Consultative services by		scores over time (less severity) in both	between intervention and control
intervention program		-delirium resource nurse		cohorts ( $p = 0.0013$ )	groups or between delirious and
for delirium on the		-geriatric nurse specialist			nondelirious patients
incidence and course		-psycho-geriatrician		On average the CAM scores decreased by	
(severity and		4. Use of a scheduled pain		0.082 units a day	Limitations
duration) of delirium,		protocol		,	-pre/post study design
cognitive functioning,		•	Cognitive function	Intervention vs control	-less control of confounding
functional			Sub-dimension memory	p = 0.0357 (see figure 4)	variables
rehabilitation,				Delirium vs no delirium	-use of medical records to
mortality, and length			Memory improvement over	p = 0.0001 (both cohorts)	obtain historical data
of stay in older hip-			time		
fracture patients.			Intervention effect on		
			memory	p = 0.0087	This study demonstrated the
Funding source(s):			Overall cognitive functioning	both cohorts <b>Delirium vs no delirium</b>	beneficial effects of an
The Ministry of Public			improved	p = 0.0001 and p 0.0026	intervention program focusing on
Health and		n = 60 pre-intervention	Delirium assessment:	See above	early recognition and treatment of
Environment of the		cohort (control)			delirium in older hip-fracture
Belgian Government		(9/1996-3/1997)	Primary outcomes	See above	patients, with the delirious
			· ····································		patients in the intervention cohort
Quality Score		Men and women (80%)			showing less severe delirium,
4		Median age 80 (12)			shorter duration of delirium, and
1 · · · · · · · · · · · · · · · · · · ·					fewer memory problems.
Risk of Bias:		Protocol			
High		Usual care			

**Conclusion**: This study demonstrated the beneficial effects of an intervention program focusing on early recognition and treatment of delirium in older hip fracture patients and confirms the reversibility of the syndrome in view of the deliriums duration and severity.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Significant differences in baseline characteristics
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Pre/post design - no blinding
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Pre/post design – no blinding
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Pre/post study with historical controls Baseline imbalances Possibility of confounding variables
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G5-Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. Multicomponent geriatric intervention for elderly inpatients with delirium: a randomized, controlled trial. J Gerontol A Biol Sci Med Sci. 2006;61(2):176-81.

Characteristics         n = 200 admitted (= 6 yr)         n = 87 intervention         Delirium assessment:         Admission screen by 2 trained study         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careening account of the study hospital         Systematic methods of careming account of the study hospital         Sys	Study.	Bonulation	Intervention Crowns		Results	Commente	
Ittalia Kit 2006       N = 2040 admitted (499 yr)       n = 8 / Tolow yr)       n = 8 / Tolow yr)       Admission screen by 2 trained study       Systematic methods of methods o	Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments	
Initial constraints       n = 82 for the lighte for instruction under the study nonput service in the	Pitkala KH 2006	N = 2040 admitted (>69 vr)	n = 87 intervention	Delirium assessment:	Admission screen by 2 trained study	Systematic methods on	
acting energing energing energing 	Finland		n = 87 follow up 3 & 6 months	CAM			
etting meralt medicinu       N = 370 carceled n = 216 accluded       Men age 823 (5.6)       Digl Span DSM // Men age 823 (5.6)       Digl Span DSM // DSM // Men age 823 (5.6)       Digl Span DSM // Men age 823 (5.6)         a add on the USM // men age same tethod       In Elso Carcele du or (15.7%) (1.6) (		3					
energi medicine units tudy Design CT       N = 279 CAM positive n = 207 Excluded       Mean age 28.8 (5.6)       DSM V Memoral Delinium Assessment Scale (MDAS)       bitW Creiteria. Delinium Assessment Scale (MDAS)       bitW Creiteria. Delinium Assessment Scale (MDAS)       bitW Creiteria. Delinium Assessment Scale (MDAS)         andomization entropic sectors       Inclusion n = 87 control       1. Accurate dx of delinium n = 87 control       DSM V Scale (MDAS)       bitW Creiteria. Delinium Assessment Scale (MDAS)       bitW Creiteria. Delinium Assessment Scale (MDAS)         signed consecutively (binded staff entropic sectors)       Inclusion n = 47 control       in Baror dappical antipoycholics C. Omprehensione sectors if the protein sectors if the pr	Setting		Men and women (75.9%)	-			
<ul> <li>(c) (c) Hospital</li> <li>(c) Hospital</li> <li>(</li></ul>	0					the study hospital	
N = 174 met DSM Vortherin n = 67 control       1. Accurate dx of delinum 2. Comprehensive griating andomization omputer generated nom numbers signed consent from they sheat closest proxy.       1. Accurate dx of delinum 2. Comprehensive griating assessment       Scale (MDAS)       Instruction that were very second groups       Instruction groups       Instruction groups       Instruction groups       Instruction groups       No id conventional neuroippics in down of abyal closest proxy.       Scale (MDAS)       Basoline characteristics       No id conventional neuroippics in down of abyal closest proxy.       Instruction instructional supplements - adatum + vitamin D - hip protectors construction in a so restruction permanent institutional care       Scale (MDAS)       Instruction groups       Scale (MDAS)       Instruction groups			Mean age 63.6 (5.6)			This intervention did not	
tudy Design CT         n = 87 intervention n = 87 central         2. Comprehensive getatric assessment assessment assessment assessment assessment assessment admit ethom output unbress signed consecutive primary outcomes         day thereafter assessment assessment assessment assessment assessment assessment assessment an 18 admission from permanent institution assessment an 24 terminal proposis at admit assessment assessment an 24 terminal proposis at admit assessment assessment assessment an 24 terminal proposis at admit assessment assesstut assessment assessment assessment asstut assessment assessmen	(6) City Hospital						
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andomization ethod endomized consent from ethod momber signed consecutively phined staff emberInclusion in favor of applicant differences in treatment in favor of applicant differences in treatment infavor othors % vs % , p interventions	Study Design	n = 87 intervention	2. Comprehensive geriatric		day thereafter	prognosis as indicated b	
andomization ethod endomized consent from ethod momber signed consecutively phined staff emberInclusion in favor of applicant differences in treatment in favor of applicant differences in treatment infavor othors % vs % , p interventions	RCT	n = 87 control	assessment			no effect on mortality,	
andomization entroper       Inclusion Age > 60 moputer generated andom numbers signed consecutively binded staff       Inclusion Age > 60 moputer generated andom numbers signed consecutively binded staff       In a favor of atypical antipsycholics - Activitional supplements - activitor witamin D - activitor witamin - activitor witamin D - activitor witamin - activitor witamin			3. Avoid conventional neuroleptics	Baseline characteristics	No significant differences between		
ethod momputer generation       Age -80 Information       Age -80 Information       Mith definition         indom numbers signed consecutions       Information       5. Physioherapy.       Significant difference in treatment interventions (% vs %, p         with definition       Significant difference in treatment interventions       In the case of full bow on the consecution         tudy Length/Start- tudy Length/Start- comprehensive entritic assessment in e30 refused screening conneultation may beat intervention       7. Of visual screening       8. Of w vs 23.9%, p - 2.001       In the case of full bow on the consecution         tudy Length/Start- tudy Length/Startudy Length/Start- tudy Length/Start- tudy Length/Star	Randomization	Inclusion	in favor of atypical antipsychotics		-	length of hospital stay	
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indom numbers       closest proxy       6. General gentatic interventions       in the case of full bows         ybinded staff       Exclusion		3		Brimary outcomos	Significant difference in treatment	With definiditi	
signed consecutively binded staff				Frinary outcomes		In the acce of full blown	
bilined staff ember         Exclusion         -calcum + vitamin D         Atypectors         69.0% vs 29.9% p. < 0.01         intervention may be Tig little to a later of 20.0% vs 20.0% p. = 0.06           tudy LengthStart- top Dates         n = 148 admission from permanent institutional care facility         -calculm + vitamin D         -hip protectors         Atypectority is 0.0% vs 20.0% p. = 0.001         intervention may be Tig little to a later definition may be Tig           vulp LengthStart- top Dates         n = 202 discharged <48 h n = 202 discharged +48 h n = 20 discharged bettor         B. Omprehensive discharge planning         -consultation with social worker -consultation with social worker -consultation with social worker -consultation with social worker -calcubre of the social worker -calcubre of the social worker -consultation with social worker -calcubre of the social worker -calcubre of the social worker -calcubre of the social worker -consultation with social worker -calcubre of the social worker -calcubre of th		ciosesi proxy					
iember       N = (see below)       -hip protectors       -hip protectors       -hip protectors       0.0% vs 23,0%, p = .006       iiitie to late' to produc         Ludy Length/Start- top Dates       -hip protectors       7. Cholmesterase inhibitors       -Actyt/cholmesterase inhibitors       8.0% vs 23,0%, p = .006       a significant difference         2001-11/2002       n = 118 admission from facility       n = 30 refused screening       0.0% vs 23,0%, p = .001       7.0% vs 9.3%, p < .001							
Mot screened (305) to put set 2001-11/2002       Not screened (305) n = 132 discharge (305) n = 202 discharge (305) n = 22 discharge (305) n = 24 terminal prognosis n = 43 terminal prognosis n = 15 n c aregiver(consent n = 129 did not meet DSM IV eriting a discharge (305) n = 15 n c aregiver(consent n = 129 did not meet DSM IV eriting a discharge (305) n = 15 n c aregiver(consent n = 129 did not meet DSM IV eriting a discharge (305) n = 83 follow (305) n = 83 follow (305) a discharge (305) n = 83 follow (305) n = 900 follow (305) n = 83 follow							
tudy Longth/Start- top Dates       n = 118 admission from particip Dates       MMSE < 23	member	N = (see below)			8.0% vs 23,.0%, p = .006		
top Dates 2001-11/2002       permanent institutional care are 2001-11/2002		Not screened (305)	<ol><li>Cholinesterase inhibitors if</li></ol>	Acetylcholinesterase inhibitors	58.5% vs 9.3%, p <.001	a significant difference i	
top Dates 2001-11/2002         permanent institutional care are comprehensive discharge J 201 structure        also MR1 or CT if cognition mained after delifium resolution 8. Comprehensive discharge planning        also MR1 or CT if cognition by the protectors Spreaded after delifium resolution 8. Comprehensive discharge planning         92.0% vs 0.0%, p - c.001 89.7% vs 4.4%, p - c.001 89.7% vs 4.4%, p - c.001 89.7% vs 4.4%, p - c.005 51.7% vs 8.0%, p - c.001 89.7% vs 4.4%, p - c.005 51.7% vs 8.0%, p - c.001 89.7% vs 4.4%, p - c.005 51.7% vs 8.0%, p - c.001 89.7% vs 4.4%, p - c.005 51.7% vs 8.0%, p - c.001 89.7% vs 4.4%, p - c.001 80.7% vs 4.4%, p	Study Length/Start-	n = 118 admission from	MMSE <23	Vitamin D + calcium	77.0% vs 9.3%, p <.001	prognosis and thus, eve	
2001-11/2002       facility       impaired after delifium resolution       Hip protectors       90.% vs.1.%, p. <0.01		permanent institutional care	-also MRI or CT if cognition	Nutritional supplements			
umposen = 202 discharged <48 h8. Comprehensive discharge planingPhysical therapy Specialist consultation8.7% vs 44.8%, p <.001delinium among such patients.o investigate whether o comprehensiven = 202 discharged <48 h							
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In a 10 permanent isstitutional care among tatients with delirium. days manent institutional care among tatients with delirium. or e 15 no caregiver/consent n = 15 no caregiver/consent n = 15 no caregiver/consent n = 12 gid not meet DSM IV the this treatment is barbelical in reducing terme these that is treatment is barbelical in reducing contraining the number of days barbelical in reducing contraining contrelificatin contraining contraining contraining contrain	treatment are effective	delirium dx confirmed	caregiver(s)			prognosis:	
and permanent       care       care       care       significant for montality       significant for montality       HR 2.1 (1.1-4.0)       29.3 (25.6) vs 22.9 (18.4), p = .171       HR 2.1 (1.1-4.0)         stitutional care among       n = 15 no caregiver/consent       n = 129 did not meet DSM IV       Criteria       HR 2.1 (1.1-4.0)       Deceased       29.3 (25.6) vs 22.9 (18.4), p = .171       HR 2.1 (1.1-4.0)         stot determine hether this treatment       beneficial in reducing       All patients protocol       Screened within 2 days of       antipsychotics and Chi       HR 0.3 (0.1-0.8)         set in institutions, level ing delinium, or proxy interview       -CAM, MMSE, Digit Span,       n = 87 control       n = 83 follow up 3 & 6 months       n = 83 follow up 3 & 6 months       n = 83 follow up 3 & 6 months       n = 83 follow up 3 & 6 months       n = 83 follow up 3 & 6 months       n = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 follow up 3 & 6 months       N = 83 foll	in reducing mortality	n = 10 permanent institutional	3 ()		No significant difference between		
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Iso to determine hether this treatment beneficial in reducing enumber of days pent in institutions, terivating definition, on proving cognition or hysical functioning of elese patients.       criteria       All patients protocol Screened within 2 days of admission (baseline)       n = 87 control n = 83 follow up 3 & 6 months n = 83 follow up 3 & 6 months n = 83 follow up 3 & 6 months n = 83 follow up 3 & 6 months n-proxy interview -premorbid dementia allowed medical record retrieval of endpoint data       Delirium assessment: med record review -premorbid dementia allowed medical record retrieval of endpoint data       Antipsychotics and Chil n = 83 follow up 3 & 6 months n = 83 follow up 3 & 6 months n = 83 follow up 3 & 6 months allowed medical record retrieval of endpoint data       Pelirium assessment: Baseline characteristics       Patience haracteristics Primary outcomes       Antipsychotics and Chil did not affect mortality Primary outcomes         Winding source(s): roomorbidities (CMI) - Follow up at 3& 7 6 months elsinki University entral Hospital, cademy of Finland - Geriatric Depression Scale - Mini-Nutritional Assessment - proxy interview       Men and women (71.3%) Mean age 83.3 (6.2)       Men and women (71.3%) Mean age 83.3 (6.2)       Men and women (71.3%) Mean age 83.3 (6.2)         uality Score: 7 isk of Bias: Unclear      Mini-Nutritional Assessment - proxy interview      Mini-Nutritional Assessment - proxy interview <td></td> <td>5</td> <td></td> <td></td> <td></td> <td></td>		5					
hether this treatment beneficial in reducing en umber of days een umber	•				34.5% vs $29.9%$ , $p = .510$		
beneficial in reducing le number of days nent in institutions, leviating delirium, or proving cognition or hysical functioning of nese patients.       I patients protocol Screened within 2 days of admission (baseline)       n = 87 control n = 83 follow up 3 & 6 months n = 4 refused assessments but allowed medical record retrieval of endpoint data       Delirium assessment: Baseline characteristics       Antipsychotics and Chi did not affect mortality         unding source(s): ions Organization, elsinki University entral Hospital, cademy of Finland       Follow up at 3&7 6 months -Hols cale -Geriatric Depression Scale -Mini-Nutritional Assessment -proxy interview       Men and women (71.3%) Mean age 83.3 (6.2)       Secondary outcomes       Secondary outcomes         uality Score: 7       -Mini-Nutritional Assessment -proxy interview       -Bathel Index -Geriatric Depression Scale -Mini-Nutritional Assessment -proxy interview       Is the third randomized trial showing no effect of geriatric intervention on the prognosis for delirium. Good, comprehensive geriatric treatment is justified in this patient group ecause of more effective alleviation of delirium and improved cognition. However, individual cases deserve careful tailoring of treatment and evaluation whether they benefit from active, curative <td></td> <td>criteria</td> <td></td> <td></td> <td></td> <td></td>		criteria					
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bent in institutions, leviating delirium, or proving cognition or hysical functioning of lese patients.       admission (baseline) -CAM, MMSE, Digit Span -prowing cognition or premorbid dementia status (CDRS; DSM IV) -med record review -comorbidities (CMI)       n = 83 follow up 3 & 6 months n = 4 refused assessments but allowed medical record retrieval of endpoint data       Baseline characteristics       Primary outcomes         unding source(s): onso Organization, elsinki University cademy of Finland       -comorbidities (CMI) Follow up at 3&7 6 months -MMSE       Men and women (71.3%) Men ang 83.3 (6.2)       Men and women (71.3%) Mean age 83.3 (6.2)       Baseline characteristics       Primary outcomes         unality Score: 7 isk of Bias: Unclear       -Mini-Nutritional Assessment -proxy interview       -Mini-Nutritional Assessment -proxy interview       n = 6fect of geriatric intervention on the prognosis for delirium. Good, comprehensive geriatric treatment is justified in this patient group ecause of more effective alleviation of delirium and improved cognition. However, individual cases deserve careful tailoring of treatment and evaluation whether they benefit from active, curative							
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<ul> <li>Ileviating delirium, or proving cognition or hysical functioning of uese patients.</li> <li>-CAM, MMSE, Digit Span - roxy interview</li> <li>-premorbid dementia status (CDRS; DSM IV)</li> <li>-med record review</li> <li>-comorbidities (CMI)</li> <li>Follow up at 3&amp;7 6 months</li> <li>elsinki University</li> <li>entral Hospital, cademy of Finland</li> <li>-Geriatric Depression Scale</li> <li>-Geriatric Depression Scale</li> <li>-Mini-Nutritional Assessment</li> <li>-proxy interview</li> <li>on = 4 refused assessments but allowed medical record retrieval of endpoint data</li> </ul>	spent in institutions,	admission (baseline)	n = 83 follow up 3 & 6 months			did not affect mortality	
nproving cognition or hysical functioning of lese patients.       -proxy interview -premorbid dementia status (CDRS; DSM IV) -med record review -comorbidities (CMI)       allowed medical record retrieval of endpoint data       Primary outcomes         unding source(s): ions Organization, elsinki University entral Hospital, cademy of Finland       -comorbidities (CMI) Follow up at 3&7 6 months -MMSE       Men and women (71.3%) Mean age 83.3 (6.2)       Primary outcomes         Usual care       Usual care       Usual care       Usual care       Usual care         onclusion: This study is the third randomized trial showing no effect of geriatric intervention on the prognosis for delirium. Good, comprehensive geriatric treatment is justified in this patient group ecause of more effective alleviation of delirium and improved cognition. However, individual cases deserve careful tailoring of treatment and evaluation whether they benefit from active, curative	alleviating delirium, or	-CAM, MMSE, Digit Span		Baseline characteristics			
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cademy of Finland       -IADL scale         -Geriatric Depression Scale         -Mini-Nutritional         Assessment         -proxy interview                 onclusion: This study is the third randomized trial showing no effect of geriatric intervention on the prognosis for delirium. Good, comprehensive geriatric treatment is justified in this patient group ecause of more effective alleviation of delirium and improved cognition. However, individual cases deserve careful tailoring of treatment and evaluation whether they benefit from active, curative	Central Hospital,	-Barthel Index					
-Geriatric Depression Scale         -Muni-Nutritional         Assessment         -proxy interview                 onclusion: This study is the third randomized trial showing no effect of geriatric intervention on the prognosis for delirium. Good, comprehensive geriatric treatment is justified in this patient group ecause of more effective alleviation of delirium and improved cognition. However, individual cases deserve careful tailoring of treatment and evaluation whether they benefit from active, curative or the second seco	Academy of Finland						
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			ved cognition. However, individual cas	ses deserve careful tailoring of trea	tment and evaluation whether they benefit		

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
• Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	No comment on blinded outcome assessment
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G3-G5-Mudge AM, Maussen C, Duncan J, Denaro CP. Improving quality of delirium care in a general medical service with established interdisciplinary care: a controlled trial. Intern Med J. 2013;43(3):270-7.

Characteristics         N = 41 calmissions         n = 62 intervention unit n = 62 intervention unit n = 62 intervention unit n = 63 calmist to delirum dx         Delirum assessment: CAM administered to all delirous and at risk profiles is streaming and the week throughout in = 74 antitist to delirum dx         No significant differences profiles is streaming and the week throughout in = 74 antitist to delirum dx         No significant differences between groups intravention (62) vs control (74)         No significant differences between groups intravention (62) vs control (74)         No significant differences between groups intravention (62) vs control (74)         No significant differences between groups intravention (62) vs control (74)         No significant differences between groups intravention or control activity vs 83 ds 3 (100 vs 98 ds 4, p = 0.02         No significant difference between groups intravention or control activity vs 83 ds 4, p = 0.02         No significant difference between groups intravention solutopics (see roomy vs returns) (MEE = 71)         No significant difference between groups intravention intravention intrevention intrevention intravention intravention intravention int	Study	Population	Intervention Groups	Measure	Results Outcome	Comments
Midge A2013 n = 209 critical (discless below) N= 206 risk streaming hospital boginal         n = 4 4 a dission n = 4 3 a trisk for delirium dx n = 4 3 at risk for delirium dx n = 7 4 control (13)         Delirium assessment: CAM         CAM administered to all delirious and at risk patients by risk for delirium dx n = 1 4 at risk for delirium dx n = 4 at risk for de		ropulation	intervention Groups	Measure	Outcome	Commenta
Australia       n = 200 excluded (see below)       n = 14 stick for delirum dx       n = 14 stick for delirum dx       n = 14 stick for delirum       N = 206 instick for delirum       N = 206 instic		N = 415 admissions	n = 62 intervention unit	Delirium assessment:	CAM administered to all delirious and at risk	No significant difference
Selecting Metropolital tables in ± 22 difficant in ± 32 difficant concurrent control in trail         n = 24 at risk for definition in ± 32 difficant in ± 32 difficant informed consent (patient or proxy)         n = 4 at risk for definition in ± 32 difficant in ± 32 difficant in ± 32 difficant informed consent (patient or proxy)         n = 4 at risk for definition in ± 32 difficant informed consent (patient or proxy)         n = 4 at risk for definition in ± 32 difficant informed consent (patient or proxy)         n = 4 at risk for definition in ± 32 difficant informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or proxy)         n = 4 at risk for definition informed consent (patient or prox)         n = 4 at risk for definition informed consent (patient or prox)         n = 4 at risk for definition informed consent (patient or prox)         n = 4 at risk for definition informed consent (patient or prox)         n = 4 at risk for definition informed consent (patient or prox)         n = 4 at risk for definition informed consent (patient or prox)         n = 4 at risk for definition prox = 4 at risk for definition proper method proprox methorin prox = 4 at risk for definition proper methor prope	Australia	n = 209 excluded (see below)	n = 19 delirium dx	CAM	patients by trained project staff within 48 h	for all intervention (62)
Setting motopilation motopilation         N = 136 at risk for delium motopilation         Mean and women (51.6%) Mean age 736 (6.2)         Mean adwomen (51.6%) Mean age 736 (6.2)         Mean adwomen (51.6%) Mean adwomen (45.6%) Mean adwomen (45.6%) Mean adwomen (45.6%) Mean adwomen (			n = 43 at risk for delirium	-		
Metrogolital teaching in = 52 admitted to intervention or ont intervention or control ital         Mean age 795 (6.2) Impaired vision or hearing inspection and women (51.8%). Baseline characteristics         Baseline characteristics         No significant difference between groups intervention (62) vs control (74)         -inpaired isolation inpaired vision or hearing inpaired vision or hearing intervention or control intervention or control intervention or control on retrievention or control on retrievention or control intervention inplementation proxy         Buseline intervention inplementation proxy         Buseline intervention inplementation proxy         Intervention (51 yr intervention (74) intervention inplementation proxy         Intervention inplementation proxy         Intervention inplementation proxy         Intervention (74) intervention (74) intervention (74) intervention inplementation proxy         Intervention (74) intervention (74) intervention inplementation proxy         Intervention (74) intervention (74) intervention inplementation proxy         Intervention (74) intervention (74) intervention inplementation proxy         Intervention proxy         Intervention proxy	Setting	g				
hospial     n = 62 admitted to intervention     Mean age 79.6 (6.2)     Basellen characteristics     No significant difference between groups     -Inpailed cognits       Study Design		N = 136 at risk for delirium	Men and women (51.6%)			
Study Design Concurrent controlled frail         unit n = 74 admitted to control units and ensetting control trail         Unit chosen because of an equation to single meeting definition presence of identifiable motanty and fails were control units         Intervention (62) vs control (74) (74) vs 58.6% (74) vs 56.6% (74) vs 56.				Baseline characteristics	No significant difference between groups	
Study Design Trail         n = 74 admitted to control units trail         n = 74 admitted to control units trail         n = 74 admitted to control units trail         n = 74 admitted to control units aconstant occupancy by admitted to intervention or control units (See detail and nursing thermaterial (MS = 56 a)s.         15.4% vs 56.8%.         The trends toward spresses 59.7% vs 50.0%.           Selection method admitted to intervention or control units of reference positive proxy)         Intervention or control units thermetrial (MS = 100 proxy)         The trends toward spresses proxy)         16.4% vs 56.8%.         The trends toward spresses proxy vs 30.4%           Study Length/Start or informed carbination severe dimenta (MS = 208 m = 27 Previously occuments (MS = 208 m = 27 Previously occuments and improve duration of detinon and improve carbination and improve carbination carbination and improve carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination carbination	noopital		mean age 70.0 (0.2)			
Concurrent controlled trial       Inclusion Admitted to intervention or control units Admitted to intervention or control units Admitted to intervention or control units and e256 Admitted to intervention or control units Admitted to intervention or control units Admitted to intervention or control units accenting       Impaired vision or the anding behridges       100% vs 98.6%       The trends toward mortally and fails we enclose and nursing champions         Selection entities provy	Study Docian		Linit chosen because of	Impaired cognition		
trial       Inclusion       Age 250       Single medical team       Detryduation       59.7% vs 50.0%       Improved in hospital         Selection method       Age 250       Admitted to intervention or control units       Anticpated LOS 3 days       medical and nursing         rintervention or control       Anticpated LOS 3 days       Intervention strategies (see drama difference between groups is a second diffication of the low incidence of detrification during and low is 0.0% vs 30.8%       The low incidence of detrification during and low is 0.0% vs 0.0%       The low incidence of detrification during and low is 0.0% vs 0.0%       The low incidence of detrification during and low is 0.0% vs 0.0%       The low incidence of detrification during and low is 0.0%       The low incidence of detrification during and low is 0.0%       The low incidence of detrification during and low is 0.0%       The low incidence of detrification during and low is 0.0%       The low incidence of an						The trends toward
Selection erfbild         Age 265		Inclusion				
Selection method intervention or control intervention or strategies (see detail Table 1)       CAM screening in the number of delinum or had 22 detail Table 1)       T.4% vs 83.8% 30.6% vs80.45. Significant difference between groups Delinious vs trisk Sock vs 43%, p = 0.008       The low incidence of delinum intervention strategies (see detail Table 1)         Study Length Study Length S	ula					
Patients admitted to intervention or control units control units       control units control units       champions       Prevaient delinum       30.6% vs36.45       intervention strategies (see detail Table 1)         Proving       p	Cala ati an math a d					
intervention or control       Anticipated LOS 23 days       given the small sample data       gi			5			
unit screening outlive for delinium on initial screening or delinium and z proxy)       Informed consent (patient or prox)       Informed consent (			champions	Prevalent delinum		
for delinum or ind al 22 delinum or ind al 22 delinum or ind al 22 delinum or ind al 22 methods       proxy)       deliai Table 1)       Apple altitum or ind 22 delinum or ind 24 delinum o						•
delifium on initial screening	•					size.
screening       Exclusion       -Delirium detection       -Delirium detection       -Delirium detection         Study Length/Star- Not described       n = 21 Critically iii       -Delirium detection       -Delirium detection       -Delirium detection         Not described       n = 27 Previously documented severe dementia (MMSE <10)		proxy)	,		83.1 vs 80.0, p = 0.02	
Study Length     N = 209     -Education and training     -Feducation and training     -Feduca			0	•		
Study Length/Start- Stop Dates       n = 21 Critically ill severe dementia (MMSE <10) n = 20	screening			acute illness	67% vs 43%, p = 0.008	
Stop Dates       n = 27 Previously documented       -Team strategies       -Team strategies       -Team strategies       -Patient/carer information         Not described						the delirious cohort and
Not described       severe dementia (MMSE <10)	Study Length/Start-					limited evidence of
n = 20	Stop Dates				34% vs 51%, p = 0.05	process improvements
Purpose To implement delinium guidelines in general medical patients to reduce incidence and and improve outcomes in delinium a 15 other n = 32 RotLenglish speaking n = 34 Not English speaking n = 34 Not English speaking n = 34 Not English speaking n = 32 RotLenglish speaking n = 3	Not described	severe dementia (MMSE <10)	-Patient/carer information	Incident delirium during		may reflect the
To implement delirium guidelines in general medical patients to and improve outcration of delirium and improve outcrations in delirious patients.       -Intellectual disability -establishment and planning -establishment and planning -orpicet staff recruitment -development of screening tools       11 days vs 8 days, p = 0.07 0% vs 0%       model of care rather -ecommendations or poor implementation -development of screening tools       model of care rather -establishment and planning -orpicet staff recruitment -development of screening tools       11 days vs 8 days, p = 0.07 0% vs 0%       model of care rather -genomendations or poor implementation         Funding source(s): Quality Score 4       Bilning Project staff were aware of group assignment       -face tother -development data -development data       Intervention (19) vs control (27) to 16 (12-20) vs 8 (4-20), p = 0.01 Trend 0% vs 18.5%, p = 0.07 NS 16 (13-26) vs 10 (4-24), p = 0.11 Trend 0% vs 18.5%, p = 0.02       Although no new deli to 0% vs 18%, p = 0.02         Quality Score 4       Analysis Confined to participants who receining       n = 74 control units n = 27 delirium dx n = 27 delirium dx n = 27 delirium dat screening       Delirium assessment: Baseline characteristics       See above       See above       Net adves data scree above         Although there was a committee Leader		n = 20		admission	0% vs 0%	effectiveness of the
guidelines in general       -Dysphasia       -Dysphasia       an 34 Not English speaking       ineffective guideline         medical patients to reduce incidence and duration of delinium and ipaning - project staff recruitment - development of screening       Destablishment and planning       32% vs 11%, p = 0.04       0% vs 0%       0% vs 0%         n = 15 other       n = 52 Refused or unable to olia proxy consent       n = 92 Refused or unable to olia proxy consent       Ok evelopment of screening       Outcomes for delirium and planning       0% vs 0%       0% vs 0%       0% vs 0%       0% vs 0%       Although no new delicase ware identified cases ware identified cases ware identified cases may the evaluation phase       -development of screening       LOS hospital stay (days)       16 (12-20) vs 8 (4-20), p = 0.01       Although no new delicases may the evaluation phase       -evaluation ph	Purpose		Intervention implementation	Trend to longer LOS		existing interdisciplinary
medical patients to duration of delinum and improve outcomes in delinious patients.       n = 34 Not English speaking n = 92 Refused or unable to obtain proxy consent equired palliding ecare Unconscious       - project staff recruitment - development of screening tois       0% vs 0%       0% vs 0%       recommendations or poor implementations or numbers and subjects       recommendations or numbers and subjects       0% vs 0%       recommendations or numbers and subjects       recommendations or numbers and subjects       n = 34 Not English speaking n = 92 Refused or unable to obtain proxy consent Quality score 4       - project staff recruitment - development of education programs       - unplementation for subjects       0% vs 0%       0% vs 0%       recommendations or numbers and subjects       recommendations or poor implementation subjects         Funding source(s): Care initiative 4       Binding project staff were aware of group assignment       recommendations or numbers and socreaning       n = 74 control units n = 74 control units n = 74 delirium dx n = 47 a trisk for delirium from intervention ward prointee Lader - consultant physician from intervention ward prointee Lader - consultant physicion from intervention ward prointee Lader - consultant	To implement delirium	-Intellectual disability	phases	(median)	11 days vs 8 days, p = 0.07	model of care rather that
medical patients to reduce incidence duration of delirium and improve outcomes in delirious patients.       n = 34 Not English speaking n = 92 Refused or unable to obtain proxy consent quarking source(s):       n = 34 Not English speaking n = 92 Refused or unable to obtain proxy consent quarking source(s):      project staff recruitment development of screening tools      project staff recruitment development of screening tools       0/% vs 0%       Intervention (19) vs control (27)       Although no new deli cases were identified cases were identified subjects         Funding source(s): Queensland Health Strengthening Aged Care initiative 4       Blinding Project staff recruitment development of education programs evaluation phase       n = 74 control units n = 74 control units n = 74 delirium dx n = 47 delirium dx n	guidelines in general	-Dysphasia		Psychogeriatric consultation	32% vs 11%, p = 0.04	ineffective guideline
reduce incidence and duration of delirium and improve outcomes in delirious and improve outcomes in delirious       n = 15 other      development of screening tools      development of screening tools       Ductomes for delirium subjects       Intervention (19) vs control (27)       Although no new deli- cases were identified cases were identifie	medical patients to	n = 34 Not English speaking	-project staff recruitment		0% vs 0%	recommendations or
duration of delinium       n = 92 Refused or unable to       obtain proxy consent       revelopment of education         and improve       outcomes in delinium       subjects       LOS acute stay(days)       16 (12-20) vs 8 (4-20), p = 0.01       cases were identified         Funding source(s):       Blinding       Project staff were aware of	reduce incidence and	n = 15 other				poor implementation.
and improve outcomes in delirious patients.       obtain proxy consent Required palliative care Unconscious       -development of education programs       subjects LOS acute stay(days) Inpatient mortality Falls       -development of education programs       Although no new delific cases were identific cases were identific inclear cases.         Quality Score 4       n = 74 control units screening       n = 74 control units ischarge of elirity were as indentific ischarge of persistently delirious patients in the intervention group.         NS 10 (12-20) vs 10 (4-24), p =	duration of delirium	n = 92 Refused or unable to		Outcomes for delirium	Intervention (19) vs control (27)	
outcomes in delirious patients.       Required patilative care Unconscious       programs - implementation phase - implementation phase - evaluation phase - evaluatin mase - evaluation phase - evaluation phase - evaluation phase -	and improve	obtain proxy consent	-development of education	subjects		Although no new deliriur
patients.       Unconscious       -implementation phase -evaluation phase       LOS hospital stay (days) Inpatient mortality Strengthening Aged Care initiative       NS 16 (13-26) vs 10 (4-24), p = 0.11 Trend 0% vs 18.5%, p = 0.07       reassessment was d only twice aweek, sc incident cases may he been missed         Quality Score 4       Analysis Confined to participants who were delificure of the participants who were assessed of -close proximity to intervention unit -similar staffing and policies       Delifium assessment: Baseline characteristics       See above       See above       Although there was a delifium bay (4 beds) the intervention grou were assigned to the beds.         Conclusion:       By implementing clinical practice guidelines for delifium on a single medical ward, there was a marked reduction in discharge of persistently delifious patients of the partistage of persisten	•		•		16 (12-20) vs 8 (4-20), p = 0.01	cases were identified
Funding source(s): Queensland Health Strengthening Aged Care initiative       Blinding Project staff were aware of group assignment      evaluation phase       Inpatient mortality Falls Persistent delirium at discharge       Trend 0% vs 18.5%, p = 0.07 NS 10.5% vs 22.2%, p = 0.16       only twice a week, sc incident cases may free scales         Quality Score 4       Analysis Confined to participants who were delirious or had ≥2 risk factors for delirium on initial screening       n = 74 control units n = 27 delirium dx n = 47 at risk for delirium disciplinary Steering Committee       Delirium assessment: n = 47 dt risk for delirium been missed       See above       See above       Delirium duration cou not be adequately assessed because oo see above         High       Intervention Multi- disciplinary Steering Committee       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       Delirium duration prioritized activities Planned specific strategies Identify/address barriers Assess progress       Output comes       See above       See above       Although there was a delirium bay (beds) the intervention group, were assigned to the beds.	patients.	Unconscious			NS 16 (13-26) vs 10 (4-24), p = 0.11	reassessment was done
Funding source(s): Queensland Health Strengthening Aged Care initiative       Binding Project staff were aware of group assignment       Incident cases may f persistent delinium at discharge       NS 10.5% vs 22.2%, p = 0.16       incident cases may f been missed         Queensland Health Strengthening Aged Care initiative       Analysis Confined to participants who were delirious or had 22 risk factors for delirium on initial screening       n = 74 control units n = 27 delirium dx n = 47 at risk for delirium       Delirium assessment: Baseline characteristics       See above       See above       Delirium duration cou not be adequately assessed because of number of participant         High       Intervention Multi- disciplinary Steering Committee Leader – consultant physician from intervention ward Prioritized activities Planned specific strategies Identify/address barriers Assess progress       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       See above       See above       Although there was a delirium by (4 beds the intervention group, were assigned to the beds.         Conclusion:       By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,						
Queensland Health Strengthening Aged Care initiative       Project staff were aware of group assignment       Project staff were aware of group assignment       Project staff were aware of group assignment       Persistent delirium at discharge       31.6% vs 70.8%, p = 0.02       Delirium duration count not be adequately assessed because on number of participant discharge         Quality Score 4       Analysis Confined to participants who were delirious or had ≥2 risk factors for delirium on initial screening       n = 74 control units n = 47 at risk for delirium assessed hecause of -close proximity to intervention unit -similar staffing and policies       Delirium assessment: n = 47 at risk for delirium n = 47 at risk for delirium n = 47 at risk for delirium n = 47 at risk for delirium screening       See above       See above       Nen and women (48.6%) Mean age 82.3 (7.7)         Men and women (48.6%) Mean age 82.3 (7.7)       Men and women (48.6%) Mean age 82.3 (7.7)       See above       See above       Although there was a delirium bay (4 beds); the intervention unit -similar staffing and policies       See above       Although there was a delirium bay (4 beds); the intervention unit -similar staffing and policies         Planned specific strategies ldentify/address barriers Assess progress       Usual care       Usual care       Usual care       Isocharge of persistently delirious patients in the intervention group,	Funding source(s):	Blinding	p			
Strengthening Aged Care initiative       group assignment       analysis       analysis       analysis       belirium duration count of the adequately assessment:       Delirium duration count of the adequately assessed because of number of participants who were delirious or had >2 risk factors for delirium on initial screening       n = 74 control units n = 27 delirium dx n = 47 at risk for delirium       Delirium assessment:       See above       Delirium duration count of the adequately assessed because of number of participants who were delirious or had >2 risk factors for delirium on initial screening       Delirium duration count of the adequately assessed because of number of participant assessment:       See above       See above       Delirium duration count of the adequately assessed because of number of participant assessment:         High       Intervention Multidiciplinary Steering       Unit chosen because of - close proximity to intervention unit - similar staffing and policies       Duit chosen because of - close proximity to intervention unit - similar staffing and policies       See above       Although there was a descret of beds.         Visual care       Usual care       Usual care       Usual care       Usual care       Usual care       Intervention in discharge of persistently delirious patients in the intervention group, there was a marked reduction in discharge of persistently delirious patients in the intervention group, the					, p	
Care initiative       Analysis       Delirium duration counts         Quality Score       Analysis       Confined to participants who were delirious or had ≥2 risk factors for delirium on initial screening       n = 74 control units n = 27 delirium dx       See above       See above       not be adequately a assessed because o o number of participant with gasses deveause of not be adequately a see above       See above       See above       See above       Although there was a delirium.         High       Intervention Multi-disciplinary Steering Committee       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       Delirium assessment:       See above       See above       Although there was a delirium.         Primary outcomes       See above       See above       See above       See above       Although there was a delirium.         Men and women (48.6%)       Men ange 82.3 (7.7)       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       Secondary outcomes       See above       See above       Although there was a delirium analysis of patients were assigned to the beds.         Visual care       Usual care       Usual care       Usual care       Usual care       Secondary outcomes a marked reduction in discharge of persistently delirious patients in the intervention group, analysis of patients were assigned to the beds.         Conclusion:       By implementing clinical pra					31.6% vs 70.8% p = 0.02	
Quality Score 4Analysis Confined to participants who were delirious or had ≥2 risk factors for delirium on initial screeningn = 74 control units n = 27 delirium dx n = 47 at risk for deliriumDelirium assessment: Baseline characteristicsSee abovenot be adequately assessed because o onumber of participant discharged with persisting delirium.Risk of Bias: HighIntervention Multi- disciplinary Steering Committee Leader – consultant physician from intervention ward Prioritized activities Planned specific strategies Identify/address barriers Assess progressIntervention on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,Conclusion:By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,	0 0 0	group doorgrinnerit		alconargo		Delirium duration could
Quality Score 4       Confined to participants who were delirious or had ≥2 risk factors for delirium on initial screening       n = 27 delirium dx n = 47 at risk for delirium n = 47 at risk for delirium factors for delirium on initial screening       See above       See above       assessed because of number of participant discharged with persisting delirium.         High       Intervention Multi- disciplinary Steering Committee       Unit chosen because of -close proximity to intervention ward Prioritized activities       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       See above       Although there was at delirium bay (4 beds) the intervention group,         Conclusion:       By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,		Analysis	n = 74 control units	Delirium assessment:	See above	
4       were delirious or had ≥2 risk factors for delirium on initial screening       n = 47 at risk for delirium       Baseline characteristics       See above       number of participan discharged with persisting delirium.         High       Intervention Multi- disciplinary Steering Committee       Intervention Multi- disciplinary Steering Committee       Men and women (48.6%) Mean age 82.3 (7.7)       Primary outcomes       See above       See above       Although there was a delirium bay (4 beds) the intervention unit -close proximity to intervention unit -similar staffing and policies       See above       See above       Although there was a delirium bay (4 beds) the intervention grou there was not specific splanned specific strategies Identify/address barriers Assess progress       See above       See above       See above       Although there was a delirium bay (4 beds) the intervention grou there was not specific splanned specific strategies Identify/address barriers Assess progress       See above       See above       See above       Although there was a delirium bay (4 beds) the intervention grou there was not specific splanned specific strategies Identify/address barriers Assess progress         Conclusion:       By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,	Quality Score			Deminum assessment.		
Risk of Bias:       factors for delirium on initial screening       Men and women (48.6%) Mean age 82.3 (7.7)       Primary outcomes       See above       discharged with persisting delirium.         High       Intervention Multi-disciplinary Steering Committee       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       See above       Although there was a delirium.         Prioritized activities       Planned specific strategies Identify/address barriers Assess progress       Usual care       Usual care       Usual care         Conclusion:       By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,       See above       Men and women (48.6%) Mean age 82.3 (7.7)	4			Basolino charactoristics	See above	
Risk of Bias:       screening       Men and women (48.6%)       Primary outcomes       See above       persisting delirium.         High       Intervention Multi- disciplinary Steering Committee       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       Value       See above       See above       Although there was a delirium.         Value       Value       Value       Value       Value       See above       See above       Although there was a delirium bay (4 beds) the intervention grout there was not specific analysis of patients were were assigned to the beds.         Conclusion:       By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,	-		II = 47 at lisk for definitin	Dasenne characteristics	See above	
High       Mean age 82.3 (7.7)         Intervention Multi- disciplinary Steering Committee       Mean age 82.3 (7.7)         Leader - consultant physician from intervention ward Prioritized activities       Unit chosen because of -close proximity to intervention unit -similar staffing and policies       Secondary outcomes       See above       Although there was a delirium bay (4 beds) the intervention grout there was not specific analysis of patients w were assigned to the beds.         Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,	Risk of Bias		Men and women (48 6%)	Primary outcomes	See above	
Intervention Multi- disciplinary Steering Committee Leader – consultant physician from intervention ward Prioritized activities Planned specific strategies Identify/address barriers Assess progress       Unit chosen because of -close proximity to intervention unit -similar staffing and policies Usual care       Secondary outcomes       See above       Although there was a delirium bay (4 beds) the intervention grou there was not specific analysis of patients w were assigned to the beds.         Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,		corooning				peroioting demium.
disciplinary Steering Committee Leader - consultant physician from intervention ward Prioritized activities Planned specific strategies Identify/address barriers Assess progress       Unit chosen because of -close proximity to intervention unit -similar staffing and policies Usual care       delirium bay (4 beds) the intervention grou intervention grou there was not specifi analysis of patients v were assigned to the beds.         Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,	ngn	Intervention Multi-	Weall age 02.3 (1.1)	Secondary outcomes	Saa ahaya	Although there was a
Committee       -close proximity to       the intervention grou         Leader - consultant physician       from intervention ward       -close proximity to       there was not specifi         Prioritized activities       Planned specific strategies       Usual care       Usual care       Usual care         Conclusion:       By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,			Lipit chasen because of	Secondary outcomes	See above	
Leader – consultant physician from intervention ward Prioritized activities Planned specific strategies Identify/address barriers Assess progress       intervention unit -similar staffing and policies Usual care       there was not specifi analysis of patients were usual care         Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,						
from intervention ward Prioritized activities Planned specific strategies Identify/address barriers Assess progress Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,						
Prioritized activities Planned specific strategies Identify/address barriers Assess progress Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,						
Planned specific strategies Identify/address barriers Assess progress       Usual care       beds.         Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,			-similar staming and policies			
Identify/address barriers         Assess progress         Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,						5
Assess progress Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,			Usual care			beds.
Conclusion: By implementing clinical practice guidelines for delirium on a single medical ward, there was a marked reduction in discharge of persistently delirious patients in the intervention group,		5				
		Assess progress				
this resulted in a longer hospital stay and there was no reduction seen in one-on-one nursing use, so the intervention was costly						the intervention group, bu

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	Unclear	Although there were no significant differences between intervention groups there were differences between delirious and at risk patients
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Allocation not concealed
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Study staff not blinded
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Baseline imbalances Possible confounders (such as infrequent CAM administration) Controlled trial; not RCT
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):	1		BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G5-Young LJ, George J. Do guidelines improve the process and outcomes of care in delirium? Age Ageing. 2003;32(5):525-8.

Study	Population	Study Process		Results	Comments
Characteristics			Measure	Outcome	
Young LJ 2003 UK	Baseline study N = 211	Collection of data from baseline	Delirium assessment: CAM	Screened for delirium using the CAM (and DSM IV criteria); no discussion of	Delirium is a poorly managed condition in
Setting	Men and women (64%)	study Data recorded	DSM IV	ongoing assessment	hospital with a high use o sedation, cot-sides,
Multicenter (5) Urban District General	Mean age 81.5 (7.3) Dementia = 47%	-delirium dx -length of stay	Baseline study characteristics	Significant differences	frequent ward moves and failure to use orientation
Hospitals	Implementation of	-use of mental test score -use of sedation	Delirium dx recorded	More often when UCS was recorded 72% vs 42.9%, p <0.001	techniques
Study Design	guidelines	-use of orientation cues (clocks and		More often when MTS attempted	Poor management of
Baseline observational study ("before");	N = 147 Med/low n = 110 Med/low before	calendars) -assessment of vision		73.4% vs 51.4%, p = 0.005	delirium is reflected in a high mortality, frequent
consensus guideline development;	n = 37 Med/ low after	<ul> <li>-assessment of hearing</li> <li>-alcohol history</li> </ul>	Cot sides associations	Significant correlations	complications and long lengths of stay
randomized	N = 189 High	-complications	(higher mortality)	37.3% vs 21.2%, p = 0.02	lengins of stay
implementation "after"	n = 101 before	-ward moves	(more falls)	43.8% vs 22.1%, p = 0.002	Guidelines alone do not
study	n = 88 after		(more pressure sores)	29.7% vs 14.4%, p = 0.014	appear to improve
		Development of guidelines	(more infections)	50% vs 24.4%, p = 0.0004	management of delirium;
Selection method		-multidisciplinary consensus	(longer LOS)	21 (11-36) vs 15 (7-28), p = 0.008	educational and
All patients meeting	Inclusion	-Literature search (MEDLINE, BIDS)	land to an ended to an eff		organizational change is
inclusion criteria Clinical data from	Age ≥65 Admitted to general	-revision of consensus to include evidence from literature search	Implementation of guidelines	Hospital allocation (before vs after) Med/low before vs Med/low after	also required
medical and nursing	medical ward	-formal multidisciplinary consensus	guidennes	N = 110 vs $37$	
notes	Admitted to elderly care	process (Delphi technique)	All measures	No significant differences before vs	
Research registrar	ward	-including caregivers of patients who	7	after	
allocated hospital to low;	Screened for delirium on	had experienced delirium			
medium, high	admission (CAM)	-high degree of agreement on all		Significant differences	
intervention		recommendations		High before vs High after	
	Exclusion	-final guidelines approved by British		N = 101 vs 88	
Study Length/Start- Stop Dates	Not discussed	Geriatrics Society	Age Hearing recorded	80.6 (7,3) vs 82,.9 (7.1) p = 0.02 5% vs 15.9%, p = 0.02	
3 months baseline		Implementation of guidelines	Tleaning recorded	5 % vs 15.9 %, p = 0.02	
3 months		-baseline study repeated in the 5		Trend toward significant difference	
implementation	Assessments	hospitals		High before vs High after	
Concurrent time periods	Usual Cognitive Status	-3 levels of intervention		N = 101 vs 88	
	(UCS)	-low = feedback of baseline data	Mean LOS (d)	16 (8-30 vs 10.5 (5-29), p 0.07	
Purpose	Mental Test Score	-medium feedback of baseline data	MTS completed	16.8% vs 27.9%, p 0.07	
To devise guidelines for	(MTS)	and distribution of guidelines to nurses			
optimal management of		and doctors -high = as medium but also		Delivium was recorded in only 26% of	
delirium in clinical practice and to evaluate		teaching sessions for nurses and		Delirium was recorded in only 26% of nursing notes and 50% of medical	
whether guidelines		doctors in each center		notes	
improve the process and					
outcomes of care.		Hospitals randomized:		There was evidence of poor	
		N = 1 low intervention		management with frequent moves	
Funding source(s):		N = 2 medium intervention		between wards and using restraints	
National Audit monies		N = 2 high intervention		(cot sides).	
Quality Score:		Process and outcomes of care recorded		There was a poor process of care as	
3		as in the baseline study		use of cot sides seemed to be related to poor outcomes	
Risk of Bias:					
High					
5					

Conclusion: Delirium is a poorly managed condition in older people and guidelines alone fail to improve the process and outcomes of care.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Significant differences between groups in baseline study and in implementation study
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Baseline study = retrospective data Implementation study unclear
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Baseline study = retrospective
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Before/after study Baseline and implementation imbalances ? presence of confounders ? RCT for implementation/ no ITT
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING =
8. Sample size ≥50 each study arm (1 point if achieved):	0		Only 37 patients in med/low after
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE =

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low ri ٠

  - High risk of bias: High risk of bias on 2 or more of 6 domains

G2-Vaurio LE, Sands LP, Wang Y, et al. Postoperative delirium: the importance of pain and pain management. Anesth Analg. 2006;102(4):1267-73.

<u>.</u>				Results	
Study	Population	Study Groups	Measure	Outcome	Comments
Characteristics	N - 222	n = 144 delirium	Delinium coccercut	The interaction to see the destruction of the s	Destancestive sein and
VaurioLE 2006	N = 333	n = 144 delirium	Delirium assessment:	Trained interviewers determined the	Postoperative pain and
JSA	n = 31 not reported in delirium vs no	Mars	CAM	presence of delirium pre-op, POD1 and	pain management
	delirium comparison	Men and women (64%)		POD2. All delirium assessments were	strategies are
Setting	N = 302 analyzed	Age ≥ 70 (n) = 36		validated by a second investigator.	independently associate
Jniversity Hospital	n = 36	Age >70 (n) = 108			with the development of
	n = 74				postoperative delirium.
Study Design		Independent in 7 IADLs			
Comparative Study	Inclusion	Yes (n) = 71	Baseline characteristics	All patients	Both the presence of
	Age ≥65	TICS score (mean) 30.9	Mean age (SD)	74 (6), range 65-96	postoperative pain and
Selection method	Elective noncardiac surgery	GDS score	Preoperative chronic pain		increased pain
Consecutive patients	Anesthesia required	0-2 = 77	Moderate at rest	27.3%	postoperatively are
scheduled for major	Expected LOS >48h	3-5 = 44	Severe at rest	17%	independent predictors
elective noncardiac	Informed consent	≥6 = 23	Moderate to severe on	11 / 0	postoperative delirium
surgery requiring		Education	movement	63.3%	postoperative definition
inesthesia	Exclusion	High school or less = 50	Preoperative oral narcotics	23%	There was an ordered
inestriesia	N = not described	HS grad or greater = 91	Freoperative oral fracotics	23 /0	
		5 5	Outrouver.		relationship between
Study Length/Start-	Not capable of providing or refusing	ASA classification	Outcomes		levels of preoperative
Stop Dates	to provide informed consent	1-2 = 60	Developed delirium post op	46% of all patients	pain and the risk for
2001-2004		3-4 = 84		Significant difference between groups	development of
	Pain measurement	Surgery type		(Bivariate analysis)	postoperative delirium.
Purpose	Structured interviews by research	Neur/ortho = 86; Urol = 14		Delirium vs no delirium (p)	
o determine whether	assistants	Gyn = 17; Vasc = 7	Age	<0.0001	Severe preoperative pa
oth postoperative	-verbal VAS	Gen/ENT/Plas = 19	Gender	0.0001	was associated with
ain and pain	-0 = no pain		Independent in 7 IADLs	0.002	greater odds of
nanagement method	-1-4 = moderate pain		TICS score	0.008	developing delirium that
ad an independent	-5-10 = severe pain		GDS score	0.03	was moderate pain.
association with the	Pain recorded		Education	0.003	nao modorato pam
levelopment of	-Pre-op		ASA classification	0.015	This finding highlights t
•	-POD1 (24 h after surgery)			0.024	importance of
ostoperative			Type of surgery	0.024	
lelirium.	-POD2 (48 h after surgery)				considering and perhap
<b>.</b>	-pain at rest	n = 158 no delirium	Delirium assessment:	See above	treating both
Funding source(s):	-pain with movement				preoperative chronic pa
VIH Grant	Significant change = ≥2 point	Men and women (42%)	Outcomes (continued)		levels and postoperativ
	increase from baseline	Age ≥ 70 (n) = 74			pain levels
Quality Score		Age >70 (n) = 84	Factors associated with	Significant difference between groups	
-	Pain management		post-operative delirium	Delirium vs no delirium	IV PCA and neuraxial
	Attending physician control	Independent in 7 IADLs	Preoperative pain at rest	0.007	analgesics conferred
Risk of Bias:	-PCA	Yes = 109	Moderate	OR 2.2 (1.2-4.0)	equal risk in the
ligh	-neuraxial (epidural or intrathecal)	TICS score (mean) 32.3	Severe	OR 3.7 (1.5-9.0)	development of deliriur
	-oral opioids	GDS score	Increase in pain POD1	OR 1.1 (1.01-1.2), p 0.002	
	-combination	0-2 = 104	Mode of postop analgesia	0.002	In contrast, patients wh
	Type and daily dose of opioids	3-5 = 38	PCA or combination (n)		received oral opioid
	recorded POD1-3		( )	109 vs 93	
		≥6 = 16	Neuraxial (n)		analgesics were at
	Type and dose of other analgesics	Education	Oral narcotics	16 vs 41	decreased risk for
	recorded	High school or less = 31	Oral narcotic use POD1	0.058	delirium vs those
		HS grad or greater = 123		86 vs 77	receiving PDA.
	Assessment covariates	ASA classification	Yes (n)	51 vs 72	
	Pre-op	1-2 = 88	Any benzodiazepine post op		All of the commonly us
	-TICS	3-4 = 70	No (n)		opioid analgesics have
	-GDS	Surgery type	Yes (n)		similar effect on the
	-ADLs and IADLs	Neur/ortho = 76; Urol = 37	Any other CNS drug post op		development of
	-comorbidities (med record and	Gyn = 17; Vasc = 11		67 vs 104	postoperative delirium.
	Charlson Comorbidity Index)	Gen/ENT/Plas = 17		69 vs 44	
	-type of surgery ASA class etc		res (II)		
				l e increase in pain levels are independent pre	

**Conclusion**: Postoperative events are more important than the type of anesthesia. Levels of preoperative pain and postoperative increase in pain levels are independent predictors of the development of postoperative delirium in elderly surgical patients. Elderly surgical patients with substantial preoperative baseline pain should be targeted for more intensive pain control or addition of adju#2nt analgesia postoperatively.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Baseline characteristics not compared except as they relate to the development of delirium; these had significant differences; other differences may confound these findings
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	Unclear	NA Observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	NA – observational study
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Original N = 333 Analysis N = 302 (no explanation of difference)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Unknown baseline differences other than as related to delirium/no delirium Unknown other confounders may be present
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

# G2-Lynch EP, Lazor MA, Gellis JE, et al. The impact of postoperative pain on the development of postoperative delirium. Anesth Analg. 1998;86(4):781-5.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	No baseline comparison between groups of delirious vs nondelirious patients
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA - Observational studies
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA - Observational studies
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Exclusions not described
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>Lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Unclear how baseline confounders may have affected results
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	0		CAM not used for all patients
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 2

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low risk of bias:
   Low risk of bias on all 6 domains

   o
   Unclear risk of bias:
   High or unclear risk of bias on 1 or more of 6 domains

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  - High risk of bias: High risk of bias on 2 or more of 6 domains

G2-Leung JM, Sands LP, Rico M, et al. Pilot clinical trial of gabapentin to decrease postoperative delirium in older patients. Neurology. 2006b;67(7):1251-3.

Chudu	<b>-</b> • •		Res	· · · ·	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Leung 2006b	N = 21	n = 9 Gabapentin group	Delirium assessment:	Trained interviewer performed	None of the patients had agitate
Denmark	n = 9 gabapentin		CAM	CAM daily based on cog test	delirium as defined by the
	n = 12 placebo	Men/women 4/5	RASS	and validated by a second	Richmond agitation-sedation
Setting		Mean age 57.2 (10.3)		investigator. Inter-rater	score.
Academic hospital.	Inclusion	<b>5</b> ( )		reliability	
	Age >45 yrs	Either gabapentin 900 mg or			Two patients (one in each grou
Study Design	Undergoing surgery	placebo was administered by mouth			had postoperative sedation
Pilot RCT - double-	involving the spine	1 to 2 hours before surgery and	Baseline characteristics	Gabapentin vs placebo	reported.
	Requiring general	anesthesia.	Dasenne characteristics	Gabapentin vs placebo	reported.
plind, placebo-	anesthesia		domographic information	na aignifiaant diffaranaa	No potiont had distinged
controlled		This dose was continued for the first	demographic information	no significant difference	No patient had dizziness,
	Stay in the hospital > 72hrs.	3 postoperative days.	Independent in 5 ADLs	8 vs 12; p=1.0	nystagmus, or ataxia.
Randomization			Independent in 7 IADLs	6 vs 7 ; p=0.43	
method	Exclusion	Intraoperative anesthetic for all	TICS score	33.6 (2.6) vs 34.5 (3.0);p= 0.47	
A computerized	N = not described	patients was standardized to IV	GDS score	3.9 (2.3) vs 6.2 (4.9); p= 0.18	Comments:
andom number list	Could not complete the	anesthetics and a low dose	Charlson Comorbidity Index	1.2(1.9) vs 0.5 (1.0); p= 0.28	In surgical pain models and in
was created	delirium testing	inhalational agent. Postoperatively,	No. preopcomorbid conditions	2.3 (1.5) vs 1.8 (1.2); p= 0.40	clinical studies of inflammatory
	Taking preoperative	all patients received on-demand	Preoperative opioid use	5 vs 8; p= 0.60	pain that produce allodynia an
Study Length/Start-	gabapentin	patient controlled analgesia		, p	hyperalgesia, gabapentin and
Stop Dates	Sensitivity to gabapentin.	(PCA) with IV hydromorphone.			analogs improve pain.
2005 - first 3	Censitivity to gabapentin.	(i or) warry nyaromorphone.	Primary outcomes		analogs improve pain.
				0/0 ( 00/) vo E/12 ( 420/)	Those findings suggest that
postoperative days	Dein sesserents		incidence of post-op delirium	0/9 ( 0%) vs 5/12 ( 42%)	These findings suggest that
	Pain assessment:			p= 0.045	sensitization of dorsal horn
Purpose	Verbal VAS (0-10) during		Preoperative vs post operative		neurons may be an important
To assess safety and	the last 24 h		VAS	no significant difference	mechanism for pain in the earl
feasibility to enable a	- at rest			between groups on any POD	postoperative period.
subsequent larger trial	-average,		Secondary outcomes		
to be conducted to	-minimum pain		Post-op PCA hydromorphone	trend toward a reduced use	In addition, antihyperalgesic
compare the incidence	-maximum pain		pain levels	similar in 2 groups	drugs could improve post-
of postoperative	·			Gabapentin vs placebo	operative analgesics, as they
delirium in patients	Assessment pre-op		Day of surgery $(n = 21)$	2.68 (2.24 vs 3.32 (3,95)	may block pathologic pain whil
given gabapentin vs .	ADL Scale: (Katz)		POD1 $(n = 21)$	2,78 (2.26) vs 13.54 (25.31)	leaving other protective
placebo and to	IADL Scale : (Lawton-Brody)		POD 2 (n = 20)	2.47 (3.65) vs 7.86 (15.20)	nociceptive mechanisms intact
					nociceptive mechanisms intact
determine if the rates of	TICS: (Telephone Interview		POD 3 (n = 17)	1.84 (2.73) vs 1.02 (2.35)	
delirium vary with	for Cognitive Status)		Time x drug	p = 0.37 (2.26)	
differences in pain	GDS: (Geriatric Depression				ļ
severity and opioid consumption	Scale) ASA classification	n = 12 Placebo group	Delirium assessment:	See above	
·	ASA classification	Men/ women 7/5	Baseline characteristics	See above	
Funding source(s):		Mean age 61.4 (11.3)			
Institutional funds and			Primary outcomes	See above	
the NIA, NIH Grant		See above	-		
#1K24 AG00948-05			Secondary outcomes	See above	
Quality Score					
5					
Risk of Bias:					
High					
iigii					

Conclusion: In this small study, gabapentin was safe and was associated with a significantly lower incidence of postoperative delirium.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Number of exclusions not described
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT analysis (low N)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		<50 total patients
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

# G1-G2-G3- Krenk L, Rasmussen LS, Hansen TB, et al. Delirium after fast-track hip and knee arthroplasty. Br J Anaesth. 2012a;108(4):607-11.

Study Population		oulation Standard Protocols	Results		Comments
Characteristics			Measure	Outcome	
Kren kL 2012	N = 225 enrolled		Delirium assessment:	Nursing staff were trained to	Comments:
Denmark	n = 84 declined to	All patients received standardized	DSM-IV	focus on symptoms of delirium	This study reports no cases of
	participate	anaesthesia and postoperative		and evaluate delirium every 8 h	PD in an elderly patient
Setting	n = 2 MMSE<24	analgesia according to the centre they		shift based on DSM-IV criteria.	population after fast-track
Multicenter	-	were affiliated to.		Inter-rater reliability and delirium	elective THA and TKA during
4 hospitals	Baseline characteristics			severity were not discussed.	hospitalization and 1–2 weeks
	reported = $225$	All patients fasted for 6 h without			follow-up. The fast-track set-u
Study Design	Follow up = $220$	solids and 2 h without clear liquids.	Baseline characteristics	N = 225	has reduced LOS from 7 to 10
prospective multicentre	n = 81  TKA		MMSE	28.6 (24–30)	days to a median of 3 days in
study	n = 144 THA	No patients were given sedative	ASA  /  /   / V	69/143/13/0	a decade after hip or knee
study	11 = 144 111A	premedication.	BMI (kg m-2)		arthroplasty.
Selection method	Men and women (51%)	premedication.	Smoking daily		artinopiasty.
		All notionto reasived standardized			This study studied only the
Not described	Mean age 69.4 (60-86)	All patients received standardized	Alcohol .2 units per day		This study studied only the
		postoperative care with well-defined	Hypertension		subset of arthroplasty patients
Study Length/Start-	Inclusion	discharge criteria	Lung disease		with MMSE >23 in a fast-track
Stop Dates	undergoing elective THA		Heart disease	- ( /	set-up.
2/2010 to8/ 2011	and TKA	Postoperative analgesia according to	Diabetes (type I/II)	1/17	
	anticipated length of stay	hospital protocol (= n patients)	Depression		Inclusion was not consecutive
Purpose	(LOS) <3 days	-opioids in PACU = 117	Length of stay (days)	2.6 (1–8)	because the research staff
To evaluate the	Age >60 yr	-oxycodone in hospital = 135			was only capable of evaluating
incidence of	ASA class I–IV.	-morphine in hospital = 77			four patients per week, and
postoperative delirium	Fluent in written and	-other opioid (ketobemidone) = 5	Primary outcomes		when this number was
(PD) after fast-track hip	spoken Danish.		incidence of delirium	No patients developed delirium	reached, no more patients
(THA) and knee				during their hospital stay	were asked to participate that
arthroplasty (TKA) with	Exclusion			0.0 (0.0–1.6%)	week.
anticipated length of	N = 86			or at their follow up visit (n=220)	
stay (LOS) of <3 days.	Anaesthetized in 30 days				A single patient had a LOS of
	n = 2 dementia [MMSE ≤		Secondary outcomes		8 days: this was due to
Funding source(s):	23]		postoperative complications	Within the first postop week	reoperation 4 days after
Supported by the	Parkinson's disease		postoperative complications	-1 = re-operation due to wound	primary surgery.
Lundbeck Foundation.	neurological disease			complications	prindry surgery.
	functional impairment.			-2 = re-operation with	Overall median LOS was 2
Quality Score				debridement	days.
2	alcohol abuse			-3 = superficial wound infection	uays.
2	daily use of hypnotics or				
Diak of Diac	anxiolytics			-2 = gastric ulcer	
Risk of Bias:	severe hearing or visual			-6 blood transfusions	
High	impairment.				
	n = 84 declined to enroll			All patients discharged to home	
				No readmissions or other	
				complications (median 12.0	
				days; range 5-36 dayus)	

48

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Observational study
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Not described exclusion
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>Lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Observational study No comparison group Unknown if confounders exist
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Single group (no comparison)
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 2

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low risk of bias:
   Low risk of bias on all 6 domains

   o
   Unclear risk of bias:
   High or unclear risk of bias on 1 or more of 6 domains

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  - High risk of bias: High risk of bias on 2 or more of 6 domains

# G2-Agostini JV, Leo-Summers LS, Inouye SK. Cognitive and other adverse effects of diphenhydramine use in hospitalized older patients. Arch Intern Med. 2001;161(17):2091-7.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Agostini 2001	N = 426	n = 114 Diphenhydramine-	Delirium assessment:	Trained RAs daily rating CAM and the	See outcomes
JSA	n = 114 diphenhydramine	Exposed Group	Confusion Assessment	MMSE score. Inter-rater reliability and	
	exposed		Method (CAM)	delirium severity were not discussed.	Comments:
etting	n = 312 diphenhydramine	Men 48 (42%)			The delirium symptoms
niversity hospital	nonexposed	Mean age 80.3 ± 5.6	Baseline characteristics	Exposed (114) vs Nonexposed(312)	reported in this study lik
Audu Dealan		Race, white: 101 (89%)	Mean ± SD APACHE II score	No significant differences $15.6 \pm 4.2$ vs $15.6 \pm 4.1$	capture more subtle and
Study Design	Inclusion	Admitted from: Home 107 (94%)	Baseline delirium risk	$15.0 \pm 4.2$ VS $15.0 \pm 4.1$	partial forms of delirium that do not meet full
rospective cohort tudy	>70 yrs	Nursing home 6 (5%)	Intermediate	87 (76%) vs 220 (71%)	delirium criteria. The CA
luuy	with no baseline delirium	Nursing nome 0 (576)	High	27 (24%) vs 92 (29%)	criteria were limited to a
Selection method	with the baseline definition		MMSE	$23.6 \pm 4.7$ vs $23.0 \pm 5.0$	time observation, where
Consecutive	Exclusion	Received a mean of 2.1 doses,	No. of medications	$5.4 \pm 3.1$ vs $5.6 \pm 3.2$	the recognition of these
dmissions of older	N = not described	with	impairment in ADLs	28 (25%) vs 70 (22%)	delirium symptoms
atients, divided into	profound dementia	97% of dose administered orally	No. of diagnoses	$8.0 \pm 2.8 \text{ vs } 7.5 \pm 2.8$	allowed the detection of
groups by	discharge or death in 48	while hospitalized. The maximum	Baseline sleeping difficulty	55 (50%) vs 141 (46%)	more subtle changes in
liphenhydramine	hrs	cumulative			cognitive functioning ov
exposure.	non-English speakers.	daily dose for any given patient	Primary outcomes	[RR, 95% CI]; n(%)	any 48-hour period
		was 100 mg.	Delirium symptoms*	1.7 (1.3-2.3]; 47 (42%) vs 75 (24%)	following diphenhydram
Study Length/Start-				P <.051	exposure.
Stop Dates			CAM delirium criteria	2.1 ( 0.9-4.7]; 9 (8%) vs 12 (4%)	-
8/1995 to 2/1998				OR: 2.3 (1.4-3.6)	The results suggest that
	Assessment:		Increased risk delirium symptoms	Use of diphenhydramine RR (CI)	the clinician's review of
Purpose	MMSE Chart review		Inattention*	3,.0 (1.5-5.9)	patient's list of daily
o examine the rate of diphenhydramine	Chart review Charlson comorbidity		Disorganized speech* Altered level of consciousness*	5.5 (1.0-29.8) 3.1 (1.6-6.1)	medications to remove "routine" or "as needed
ise in a large	scores			2.3 (1.1-4.5)	sleep" prescriptions is
prospective cohort of	APACHE II		Abnormal psychomotor activity* Altered sleep wake cycle*	2.0 (1.2-3.3)	critically important in
elderly hospitalized	ADL		Behavioral disturbance*	5.6 (1.0-29.2)	reducing unwanted
patients; to evaluate	, DE		Denavioral disturbance	0.0 (1.0 20.2)	outcomes such as
otential adverse			Secondary outcomes (other		cognitive decline.
outcomes (eg,			risks)	RR (CI)	
ognitive, behavioral,			New urinary catheter*	2.8 (0.4-4,.19)	This study derived
and other			Length of stay >7 d*	1.3 (1.0-1.6)	strength from the
anticholinergic			Diphenhydramine doses	237 (mean 2.1 doses/patient)	prospective cohort desig
effects) associated				<ul> <li>-24% were given inappropriately)</li> </ul>	that provided precise da
vith diphenhydramine				-50 doses for transfusion prophylaxis	on exposures, eliminate
ise; and to describe			<ul> <li>* multiple logistic regression</li> </ul>	-6doses to patients with obstructive	recall bias, and provided
current			model	urinary symptoms	carefully documented
diphenhydramine use			controlled for age, sex, and	Dose response + significant trend	outcomes from daily
n the study cohort.			baseline, delirium risk (all significant p <.05)	toward cognitive decline and increasing dosage	interviews.
unding source(s):		n = 312 Diphenhydramine-	Delirium assessment:	See above	One limitation of this stu
VIA RO1AG12551		Nonexposed Group	Deminum assessment.		was the difficulty in
P60AG10469		Nonexposed Group	Baseline characteristics	See above	controlling for other
(24AG00949		Men 119 (38%)			concurrently administer
DF98-105		Mean age 79.6 ± 6.4	Primary outcomes	See above	pharmacotherapies duri
Quality Score		Race, white: 261 (84)			hospitalization.
		Describe intervention	Secondary outcomes	See above	
		Admitted from:			
Risk of Bias:		Home 288 (92%)			
Jnclear		Nursing home 21 (7%)			
		Did not receive diphenhydramine			
		during hospitalization			
	1		1	ne and other adverse effects with a dose re	

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Unclear	NA-prospective cohort, but no significant differences in baseline characteristics between groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ol> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ol>	0	Unclear	NA-observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the <u>criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

# G2-Marcantonio ER, Juarez G, Goldman L, et al. The relationship of postoperative delirium with psychoactive medications. JAMA 1994;272(19):1518-1522.

		Results				
Study Characteristics	Population	Study Groups	Measure	Outcome	Comments	
Marcantonio ER 1994	N = 1341 in prospective	n = 91 developed delirium	Delirium assessment:	Delirium dx by meeting criteria on ≥1 day	Medication exposure	
JSA	cohort	during post op days 2-5	CAM	after the first postop day. CAM	(all patients)	
	N = 245 delirium +no delirium		MEDICUS	administered daily by trained study	Narcotics = 94%	
Setting	n = 91 delirium	Men and women (50%)		personnel post op days 2-5. In addition,	Benzodiazepines = 13%	
Jniversity Hospital	n = 154 no delirium	Mean age 73 (8)		altered mental status in both the medical	Anticholinergics = 9%	
General, Orthopedic				record and in MEDICUS on the same day	3	
and Gynecologic	Inclusion	Daily structured interviews by			There was no	
Surgery Depts)	Age >50	study personnel (days 2-5	Baseline characteristics	No significant differences between groups	interaction between the	
burgery Depts)	Major elective non-cardiac	postop; or day before	Buschine characteristics	in preoperative risk factors	associations of drug	
Study Design	procedures	discharge if before 6 days)	Primary outcomes		exposure with delirium	
				De linium un ne de linium		
Prospective cohort	Hospital stay ≥2 days	-designed to test orientation	(matched analysis)	Delirium vs no delirium	and the preoperative	
nested case control		and attention		Differences between groups	delirium risk scores.	
	Exclusion	Mental status based on		% vs %, OR (CI) (risk for delirium)		
Selection method	N =	medical record (MEDICUS	Narcotics (class)	95% vs 94%; 1.4 (0.5-4.3)	Postoperative	
Cases and controls	Not described	instrument)	Meperidine	65% vs 42%; 2.7 (1.3-5.5)	exposures to	
derived from a			Morphine	24% vs 34%; 1.2 (0.6-2.4)	meperidine and	
prospective cohort study	Preoperative evaluation	Medication exposures recorded	Fentanyl	10% vs 9%; 1.5 (0.6-4.2)	benzodiazepines were	
of patients consenting to	-medical hx review	for the 24 h before delirium	Oxycodone	10% vs 19%; 0.7 (0.3-1.6)	independently	
preoperative evaluation	-physical exam	developed	Codeine	7% vs 7%; 1.1 (0.4-3.6)	associated with the	
	-functional status testing	actoropod	Epidural administration	64% vs 42%; 2.3 (1.2-4.4)	development of deliriur	
Study Length/Start-	-cognitive status testing		Meperidine (epidural)	57% vs 34%; 2.4 (1.3-4.4)	within the next 24	
Stop Dates	-laboratory tests		Fentanyl (epidural)	5% vs 8%; 0.9 (0.3-2.7)	hours.	
1/1990-3/2002	-laboratory tests			570 vs $670$ , $0.9$ ( $0.3-2.7$ )	nours.	
1/1990-3/2002	To other in other sector		Patient controlled	220(		
•	Testing instruments		administration	22% vs 32%; 1.1 (0.5-2.2)	Although epidural	
Purpose	Specific Activity Scale		Meperidine (PCA)	4% vs 3%; 2.1 (0.4-10.7)	analgesia was	
To determine whether	Telephone Interview for		Morphine (PCA)	18% vs 29%; 0.9 (0.4-1.9)	associated with	
post-operative	Cognitive Status (TICS)			NOTE: p value not provided for narcotics	delirium, it appears the	
exposures to certain					association may be	
nedications were	Medication classes studied		Benzodiazepines (class	21% vs 8%; 3.0 (1.3-6.8), p <.01	related to the use of	
ndependently	Narcotics		Long acting	7% vs 2%; 5.4 (1.0-29.2) Long vs short	meperidine in 85% of	
associated with delirium,	Benzodiazepines		Short acting	14% vs 6%; 2.6 (1.1-6.5) p = .02	patients receiving	
after controlling for pre-	Anticholinergics		High Dose	11% vs 3%; 3.3 (1.0-11.0) High vs low	epidural analgesia.	
operative risk	5 5 5 5		Low dose	10% vs 5%; 2.6 (0.8-9.1) p = .03		
	Preoperative Risk Factors		2011 0000	.e,e te e,e, <u>-</u> .e (e.e e) p .ee	The matched design of	
Funding source(s):	independently associated		Anticholinergics (class)	11% vs 8%; 1.5 (0.6-3.4), NS	this study controlled for	
Grant funding	with postoperative delirium		Diphenhydramine	10% vs 6%; 1.8 (0.7-4.5), NS	confounding by known	
-Agency for Health			. ,		preoperative risk factor	
	(for matching controls)		High dose			
Care Policy and	Age		Low dose	8% vs 5%; 1.5 (0.5-4.1), NS <i>p</i> = .66 <i>N</i> S	for delirium and by	
Research	Poor cognitive function	n = 154 no delirium (controls)			studying only surgical	
-National Research	Poor physical function	1 or 2 selected controls who	Delirium assessment:	See above	patients, although	
Service Award for	Self-reported alcohol abuse	did not have delirium matched			neither of these	
Research in Primary	Abnormal preop serum	for each case based on the	Baseline characteristics	See above	eliminates all potential	
Care Medicine	-sodium	same preoperative risk for			confounding .	
-Established	-potassium	delirium (if >2 patients	Primary outcomes	See above		
nvestigator Award	-glucose	matched, 2 randomly selected)	-		By limiting the exposure	
AHA)	Aortic aneurism surgery		Secondary outcomes	See above	window to the 24-hour	
,	Noncardiac thoracic surgery	Men and women (50%)			period before delirium	
Quality Score		Mean age 73 (8)			developed, this study	
					tried to eliminate	
		Daily structured interviews (ass			medication exposures	
Diak of Diag		Daily structured interviews (see				
Risk of Bias:		above)			given in response to	
Jnclear		Medication exposure (see			delirium.	
		above	1			

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – case control design
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	NA – case control design
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Possible confounders (despite attempts to control for them)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G2-Taipale PG, Ratner PA, Galdas PM, et al. The association between nurse-administered midazolam following cardiac surgery and incident delirium: an observational study. Int J Nurs Stud. 2012;49(9):1064-73.

Study	Population	Study Groups		esults	Comments	
Study Characteristics	Population	Study Groups	Measure	Outcome	Comments	
Taipale PG 2012	N = 187 invited to participate	n = 54 Liberal delirium	Delirium assessment:	MMSE performed before surgery. 4	The dosage of	
Canada	n = 33 refused or lost before	group	CAM-ICU	trained study nurses administered CAM	midazolam	
	consent	5		-ICU 12 to18 h after admission to ICU	hydrochloride	
Setting	N = 154 consented	Men and women (37.0%)		and daily post op. Medical records were	administered to cardia	
tertiary care center	n = 32 excluded before surgery	Mean age 69.7 (8.3)		reviewed. The "conservative delirium"	patients is associated	
tertiary care certier	(see below)	Wear age 03.7 (0.3)		required a physician's notes. Inter-rater	with the incidence of	
Study Decian	N = 139 had surgery					
Study Design	n = 14 excluded due to	"Liberal" definition of delirium		reliability not determined; severity not	delirium independent o	
Observational study				discussed	age and other risk	
<b>.</b>	exclusion criterion	wherein patients were			factors.	
Selection method	n = 1 withdrew	classified as having delirium		Conservative classification		
Divided into 2 groups	n = 2 incomplete data	if:	Baseline characteristics	Delirium vs no delirium	Few established risk	
by whether have	N = 122 analyzed	(a) they had a physician's	Age	69.2 (8.3%) vs 65.3 (9.7), p = .02	factors for delirium we	
delirium		notation of delirium or		Liberal delirium vs no delirium	significantly associated	
	Total sample:	(b) they had a positive CAM-	Age	69.7 (8.3%) vs 64.5 (9.6%), p = .01	with delirium in this	
Study Length/Start-	Men and women (26.2%)	ICU assessment and no	Gender (male)	34 (63.0%) vs 56 (82.4%), p = .03	sample.	
Stop Dates	Mean age 66.8 (9.4)	mention of a physician's	· · · · · · · · · · · · · · · · · · ·			
4/2009 to 10/ 2009		diagnosis	Baseline significant risk factors	Liberal delirium vs No-delirium	Limitations	
1/2000 10 10/ 2000	Inclusion	alagitoolo	Peripheral vascular disease	12 (22.2) vs 4 (5.9) p = .02	-sample size not	
Purpose	Cardiac surgery			$12(22.2)$ $\sqrt{3}$ $+(0.0)$ $p = .02$	achieved	
•	-CABG				-inter-rater reliability of	
To examine the					,	
relationship between	-aortic valve repair or	n = 68 Non-delirium group	Primary outcomes	07 (00 40)	study nurses not	
nurses' PRN	replacement		CAM-ICU delirium	27 (22.1%)	determined	
administration of	Cardiopulmonary bypass	Men and women (17.6%)	Physician notes delirium	46 (37.7%) (conservative)	-anesthetic and opiat	
midazolam	expected to be used during	Mean age 64.5 (9.6)	CAM-ICU + physicians notes	71.3% agreement	agents administered in	
hydrochloride to	surgery		Midazolam dosages	22.1% no midazolam	the operating room	
cardiac surgery	Informed consent			26.2% >6.0 mg	were not taken into	
patients during the		See above	Midazolam increased delirium risk	OR (CI)	account and may have	
immediate post-	Exclusion		Conservative	2.23 (1.06-4.70)	influence sedation	
operative period and	N = see above		Liberal	2.00 (0.96-4.13)	levels.	
the development of	Emergency surgery within 12 h					
post-operative	of diagnosis		Multivariate logistic regression		The administration of	
delirium.	Cognitive impairment (MMSE)		risk factors		midazolam should	
	Not English speaking		Conservative delirium	OR (95%CI), p	involve accurate	
Funding source(s):	Visual impairment		Midazolam	1.08 (1.00–1.16), p=.04	assessments and	
Vancouver General	Required hemodialysis					
			Age	1.05 (1.01–1.10), p=.03	explicit goals for	
Hospital School of	preoperatively				sedation.	
Nursing Alumnae	Hx substance misuse		Liberal delirium			
Association	Self-reported alcohol use >7		Midazolam	1.07 (1.00–1.14), p=.06 (NS)	Undesirable patient	
	drinks/week		Age	1.07 (1.02–1.12), p=.01	behavior should never	
Quality Score			Peripheral vascular disease	4.52 (1.31–15.59), p=. 02	be the rationale for	
3	All Patients Protocol:				extensive use of	
	Midazolam (0.5–2 mg every 6			NOTE: CAM-ICU may have identified	sedation.	
Risk of Bias:	min, PRN); median dose 3.0 mg			some patients with the hypoactive form		
High	-included in a set of physicians'			of delirium. Both approaches likely		
·	standing orders			possessed some measurement error of		
	-pre-printed and added to each			unknown magnitude		
	patient's medical record.					
	-nurses administered the drug					
	following assessment of their					
	patients' sedation levels and					
	general status.				l	
				ld be administered with caution because the		
				Nurses' decisions regarding sedation admi	nistration must be	
nformed by empirical k	nowledge accurate assessment data	a and clear rationale with conside	eration of how these actions may contrib	ute to the development of delirium	55	

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences in baseline data/risks
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observational study.
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observational study.
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	High	High % exclusions (post consent); dropouts
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Baseline imbalances Possible confounders noted by authors (see limitations above)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G2-Luukkanen MJ, Uusvaara J, Laurila JV, et al. Anticholinergic drugs and their effects on delirium and mortality in the elderly. Dement Geriatr Cogn Dis Extra. 2011;1(1):43-50.

Study	Population	Study Groups		Results	Commonto
Study Characteristics	•	Study Groups	Measure	Outcome	Comments
Luukkanen MJ 2011 Finland Setting Multicenter 2 geriatric hospitals (7 acute wards) 7 nursing homes (13	N = 425 n =. 230 acute geriatric wards n = 195 nursing home residents. n = 341 $\ge$ 2 DAPs n = 84 < 2 DAPs	n = 341 ≥ 2 DAPs Men and women (83%) Mean age 86.7 (6.8) Primary school or less: 52.4% Widowed: 56.1 %	Delirium assessment: DSM-IV criteria	Trained geriatricians rated delirium based on cog test (MMSE, digital span, CDR) with diagnosis according to DSM-IV criteria. The criteria for delirium according to the DSM-IV were operationalized to simple yes/no questions and included in a questionnaire.	Over 80% of the patients in this study were using multiple DAPs as part of their everyday medication. DAP users were older and had more comorbid disease and they used more drugs than the non-
wards) Study Design Cross-sectional Selection method Participants were divided into two groups according to their use of drugs with anticholinergic properties (DAPs): subjects receiving ≥ 2 DAPs and < 2 DAPs. Study Length/Start-Stop Dates Not described Purpose To investigate the use of drugs with anticholinergic	Inclusion >70 yrs Using DAPs on a regular basis Exclusion N = not described Age <70 Coma Other assessment: Mini-Mental State Examination (MMSE) Digit Span Clinical Dementia Rating (CDR) Wechsler Adult Intelligence Scale -proverb part (testing		Age Dependent in ADL Mean MMSE (SD) Mean number of medications Charlson Comorbidity Index Delirium by DSM-IV 2 Residence -Acute geriatric ward (n = 230) -Nursing home (n = 195) 2-year mortality dementia patients mortality Primary outcomes Logistic regression Use of DAPs predicts delirium	DAP user ≥2 vs DAP user <2 Significant difference between groups 86.7 (6.8) vs 83.7 (7.2), p<0.001 74.9 % vs 83.1%, p= 0.11 13.3 (7.9) vs 11.3 (7.6), p=0.045 8.9 (3.0) vs 6.1 (3.1), p <0.001 2.4 (1.6) vs 1.5 (1.2), p<0.001 57.2 % vs 71.4%, p= 0.017 7.0 % vs 16.7%, p= 0.050 p=0.021 56.9% vs 43.1% 42.9% vs 57.1% 49.3% vs 35.7%, p=0.026 50.8% vs 31.7%, p=0.009 Significant differences OR 1.67, (0.87–3.2) (Adjusted for age, gender, and Charlson Comorbidity Index)	users. Therefore, the higher prevalence of delirium and the worse prognosis among the DAP users compared with the non-users was expected. This study failed to show an independent prognostic significance for DAP use, The negative results should be interpreted with caution. -almost all subjects used at least 1 DAP -neither the short-term nor the long-term anticholinergic effect could be quantified in this setting - DAPs are only one of the precipitating factors for delirium and their influence may be
properties (DAPs) and their associations with delirium and mortality among elderly patients with comorbidities. Funding source(s): Not disclosed	abstract thinking and judgment) Medical chart review by 2 investigators ADLs All medications DAP lists in PDF (see p	n = 84 < 2 DAPs Men and women (76.2 %) Mean age 83.7 (7.2) Primary school or less: 52.2 % Widowed: 46.8%	Risk factors Cox proportional hazard model: Charlson Comorbidity Index Age	Independently associated with mortality HR 1.18, (1.08–1.29); p < 0.001 HR 1.06/year, (1.04–1.08); p< 0.001	masked by other triggers. -it is challenging to show an independent role for any single factor -the statistical power of the study may not be sufficient to show differences between the groups.
Quality Score 3 Risk of Bias:	45) -high anticholinergic properties -detectable anticholinergic properties		Male gender	HR 1.55, (1.09–2.20); p = 0.014 <i>Not associated with mortality</i>	The use of DAPs was more prevalent among patients without dementia compared to those with dementia.
High	Preexisting dementia -global judgment of 3 geriatricians -existing dx -CDR Scale -nurse/caregiver interviews -CT/MRI imaging -previous MMSE scores		Use of DAPs	HR 1.12, (0.75–1.68); p = 0.56.	Limitations -cross-sectional design -confounding factors not controlled -variable anticholinergic properties of drugs rx

**Conclusion**: We did not find a correlation between increased mortality or increased incidence of delirium with DAP treatment. Because the use of DAPs is very frequent among frail inpatients with comorbidities, these medications should be used with caution and at a minimum dosage, especially in patients with comorbidities or dementia.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences between groups
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Cross-sectional study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Cross-sectional study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Specific numbers not described
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Cross-sectional study Funding not disclosed Likely confounders noted by authors
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G2-Gamberini M, Bolliger D, Lurati Buse GA, et al. Rivastigmine for the prevention of postoperative delirium in elderly patients undergoing elective cardiac surgery--a randomized controlled trial. Crit Care Med. 2009;37(5):1762-8.

			Results			
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects	
Samberini 2009	N = 348 assessed	n = 59 rivastigmine 1.5 mg/dose	Delirium assessment:	Study nurses and RAs rated	Placebo vs Rivastigmine	
Switzerland	n = 228 excluded	n = 0 lost to follow up	Confusion Assessment	CAM daily based on cog	(No significant difference)	
		n = 7 discontinued intervention	Method (CAM)	testing (MMSE, CDT) days 1-6.	Deatha 1 (2) vs 1 (2)	
Setting	N = 120 randomized	n = 1 death		Inter-rater reliability and	Perioperative strokea 2 (3) vs	
Jniversity Hospital	n = 59 rivastigmine	n = 6 withdrew from study		delirium severity were not	(2)	
	n = 61 placebo			discussed.	Seizuresa 1 (2) vs 0 (0)	
Study Design		N = 56 analyzed		aloodoodal	Nausea 32 (52) vs 40 (68)	
Double-blind,	Inclusion	n = 3 excluded from analysis (assess-	Baseline characteristics	Rivastigmine vs Placebo	Vomiting 24 (39) vs 27 (46)	
andomized, placebo-	>65 vrs	ment with CAM not possible)		N = 56  vs  57	Anorexia 41 (67) vs 39 (66)	
controlled trial	undergoing		SAPS II	40 (15–60) vs 34.5 (18–67)	Diarrhea 6 (10) vs 7 (12)	
	elective cardiac surgery	Men 37 (66%)	MMSE	28 (23–30) vs 28 (23–30)	Dyspepsia 5 (8) vs 4 (7)	
Randomization	cicolive baralab surgery	Mean age 74.1 (5.2)	CDT	6 (2–6) vs 6 (2–6)	Abdominal pain 8 (13) vs 8 (14	
method	Exclusion	Coronary artery bypass grafting: 30	ODT	0 (2-0) V3 0 (2-0)	Vertigo 24 (39) vs 28 (47)	
performed by the	N = 228	(54%)	Primary outcomes		Headache 6 (10) vs 7 (12)	
nospital pharmacy	Did not meet inclusion	(3478)	Delirium incidence	18 vs 17, p= 0.8	Tremor 3 (5) vs 5 (8)	
using a computer-	criteria, n = 117	Participants received placebo or	Deminum incluence	10  vs  17, p = 0.0	Insomnia 24 (39) vs 33 (56)	
		rivastigmine 1.5mg every 8 hrs, starting	Secondary outcomes		Rash 0 (0) vs 0 (0)	
generated sequence n blocks of 20	Refused to participate, n = 92	on the evening preceding the operation	MMSE BL: d 2	1(2,10) $1(4,10, -10)$		
II DIOCKS OF 20	-		CDT BL: d2	1 (-3-16)) vs1 (-4-16, p= 1.0	Sweating 28 (46) vs 25 (42)	
Studie Law with (Ctart	Other reasons, n = 19	and continuing through the intra-op and peri-op until the evening of the 6th		0 (-1–6) vs 0 (-3–6). p=0.9	Atrial fibrillation 26 (43) vs 22	
Study Length/Start-			use of a rescue treatment	47/50	(37)	
Stop Dates	Excluded from analysis	postoperative day, i.e., a total of 22	- haloperidol	17/56 vs18 /57, p =0.9	Life-threatening arrhythmia 3 (	
first 6 days pos-op	n = 7 (assess-ment with	doses. Patients are usually transferred	- lorazepam	35/56 vs 38/57, p =0.6	vs 3 (5)	
2/2006 to 7/2007	CAM not possible)	to the normal ward, 48 hours after their	duration of delirium	2.5 (1–5) vs 3 (1–6), p=0.3	Pacemaker >1 day 24 (39) vs	
_		operation.	hospital days	13 (7–39) vs 13 (7–39), p=0.3	(25)	
Purpose			days spent in the ICU.	2 (2–7) vs 2 (2–6), p=0.9		
Tested the hypothesis		After diagnosed delirium, rescue				
that prophylactic	Other assessment:	treatment consisting of haloperidol with			Comments:	
short-term	Mini-Mental State	or without lorazepam was started at			In this study, 56% of the patier	
administration of oral	Examinations (MMSE)	doses according to clinical discretion			complained of nausea and 429	
rivastigmine, a	clock drawing			• ·	suffered from postoperative	
cholinesterase	tests (CDT)	n = 61 placebo	Delirium assessment:	See above	vomiting even in placebo group	
nhibitor, reduces the	Simplified Acute	n = 1 lost to follow up			Therefore, transdermal	
ncidence of delirium	Physiology Score (SAPS	n = 7 discontinued intervention	Baseline characteristics		application of rivastigmine coul	
n elderly patients	II)	n = 1 death			have been an advantage.	
		n = 6 withdrew from study	Primary outcomes		However, at the time of the stu	
Funding source(s):					transdermal rivastigmine was r	
unrestricted research		N = 57 analyzed	Secondary outcomes		available.	
grant from Novartis		n = 4 excluded from analysis (assess-				
Switzerland		ment with CAM not possible)				
Quality Score		Men 40 (70%)				
6		Mean age 74.4 (5.9)				
		Coronary artery bypass grafting: 29				
Risk of Bias:		(51%)				
High		()				
5		See above				
		000 00010		1		

**Conclusion**: This negative or, because of methodologic issues, possibly failed trial does not support short-term prophylactic administration of oral rivastigmine to prevent postoperative delirium in elderly patients undergoing elective cardiac surgery with cardiopulmonary bypass.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out 30/120 (25%) Exclusions after randomization
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Drug company sponsorship
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G2 G4 Liptzin B, Laki A, Garb JL, et al. Donepezil in the prevention and treatment of post-surgical delirium. Am J Geriatr Psychiatry. 2005;13(12):1100-6.

Study	Population	Intervention Groups	<u> </u>	Results	Adverse Effects
Characteristics	personon		Measure	Outcome	
_iptzin 2005	N = 90 randomized	n = 39 5 mg donepezil	Delirium assessment:		Not discussed
JSA	n = 10 dropouts		Delirium Symptom	RAs did daily DSI and CAM. Based	
JOA	-not operated	Men and women (64%)	Interview	on this, co-investigator gave delirium	
Setting	-did not take study meds	Mean age 66.8 (8.9), 52-81	Confusion Assessment	rating based on DSN-IV criteria	
	n = 39 donepezil	Mean age 00.0 (0.9), 52-01	Method	rating based on Don-IV chiena	
n patient (academic		Dependentil/placeba administered with	DSM IV criteria		
nedical center)	n = 41 placebo	Donepezil/placebo administered with breakfast for 14 days before and 14			
Study Design	Inclusion	days after surgery			
RCT – double blind,	Age ≥ 50	Subjects were in charge of their	Baseline	Donepezil vs placebo	
placebo controlled	Elective total knee or hip	medication throughout their	characteristics/measures	No significant differences	
	arthroplasty	participation		Both groups cognitively intact	
Randomization		<ul> <li>Tracked study drug use on a case</li> </ul>	MMSE	Average 29/30	
nethod	Exclusion	report form in the hospital and at home	Clock Drawing Test	Average 9/10	
Randomized separately	N = 187	(forms reviewed by the research			
by a research	Evidence of GERD	assistant)			
pharmacist; subjects,	Sick sinus syndrome	Admitted 24h before surgery (preop	All outcomes (ITT	Donepezil vs placebo	
nvestigators, research	Additional 19 excluded	assessment)	analysis done)	No significant differences between	
assistant, orthopedic	Younger than 50	Delirium Symptom Interview		groups (NS) (p)	
nursing staff blinded to	Taking donepezil	Confusion Assessment Method	Subdromal delirium	71.8% vs 65.8% (0.57)	
study drug condition	Previously intolerant to	DSM IV criteria	Mean duration	1.71 d vs 2.04 d (0.28)	
study drug condition					
	donepezil	Delirium assessed east postop day	Delirium	20.5% vs 17.11% (0.69)	
	Non-English speaking	(as above)	Mean duration	1.0 d vs 1.3 d (0.12)	
Study Length/Start-	Participating in another	Called days 7 and 14 to assess new	Mean (SE), range LOS		
Stop Dates	orthopedic study	or residual symptoms of delirium	(days)	4.4 (0.13), 4-8 vs 4.2 (0.8) 4-7, (0.09)	
5/2000 to 4/2003		(collateral source information nor	Disposition to rehab	72% vs 83%, (0.23)	
	All patients protocol:	required)	Discontinued study drug		
Purpose	Operations performed by 1 of		after randomization	28% vs 27% (0.89)	
To determine whether	2 orthopedic surgeons				
onepezil would reduce	Informed of study in outpatient				
he incidence or	office	n = 41 placebo	Delirium assessment:		
duration of	Sent letter to contact study		See above		
postoperative delirium,	coordinator	Men and women (51%)			
as defined by DSM-IV	1038 patients contacted	Mean age 67.6 (8.6), 51-90			
and that donepezil	732 did not follow up or				
would reduce hospital	refused to participate	See above			
ength of stay or the	-concern about surgery				
number of transfers to	-leery of side effects				
		n = 0.40 non norticle stine estimat			4
sub-acute, short term	-relatives did not support	n = 948 non participating patients	Significant differences		
killed nursing or	participation		between participating		
ehabilitation facilities	306 patients invited to half-day	Men and women (65%)	and non participating		
	education session (2-3 weeks		patients	Participants vs nonparticipants	
unding source(s):	before surgery)		Age	2.2y younger [67.2 (8.70 vs 69.4 (8.9),	
Pfizer	-screening process			p 0.03	
	-informed consent			No other significant differences	
Quality Score	-randomization			-	
5	After enrollment				
	-MMSE				
Risk of Bias:	-Clock Drawing Test				
High					
-					
Comments: Although all	randomized patients were include	d in the analysis, only 58 patients actually of	completed the study. Adherend	e to study medication was poor. More the	an 25% of both groups
	s of the assigned drug. There were	e no significant differences between groups	s for the study completers. Eve	n when symptoms of delirium appeared, t	hey were relatively mi
ind brief.					
				lelirium or at higher risk of developing it.	

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	·
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Adherence poor Dropouts not described; very high (28% donepezil vs 27% placebo)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Pfizer funded
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		<50 both arms; 25% dropouts after randomization
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

G2-Marcantonio ER, Palihnich K, Appleton P, Davis RB. Pilot randomized trial of donepezil hydrochloride for delirium after hip fracture. J Am Geriatr Soc. 2011;59Suppl 2:S282-8

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Marcantonio ER 2011 USA Setting _arge academic medical center Study Design	N = 93 eligible for screen N = 60 approached for participation n = 16 enrolled Inclusion >70 yrs Hip fracture	n = 7 Donepezil group (5 mg) n = 1 withdrawal (after week 2) Men and Women 5 (71%) Mean age 88.0 ± 5.2	Delirium assessment: CAM Memorial Delirium Assessment Scale (MDAS). Delirium Symptom Interview (DSI)	Trained RA rated CAM daily based on cog test (MMSE, digital span). MDAS for delirium severity.	Side Effects: Donepezil vs Placebo Insomnia 5/7=71% vs 1/9=119 p=0.04 Diarrhea 3/7=43% vs 0/9 p=0.06 Nausea 2/7=29% vs 2/9=22% p=1.0
Pilot RCT: double- masked placebo- controlled Randomization method Permuted block scheme stratified on dementia Study Length/Start- Stop Dates 30 days 1/2007 to 8/2008 Purpose To determine whether donepezil hydrochloride can reduce the prevalence and severity of delirium among older patients undergoing hip fracture repair. Funding source(s): NIA R21 AG027549 K24 AG035075 Quality Score 5 Risk of Bias: Unclear	English speaking Adequate hearing Informed consent (patient or proxy) Exclusion N = 44 44 refused -14 unwilling to take additional medication -7 unwilling to incur added burden of study -5 unwilling to participate in any research -4 specific concerns about donepezil -1 inability to contact caregiver for consent Stratified design Controlled for any effect donepezil might have on underlying dementia rather on delirium Dementia assessed from the medical record and Informant Questionnaire for Cognitive Decline Protocol for all patients: All hip fracture patients at our medical center are admitted to a geriatrics-orthopedics service, and therefore receive perioperative co-management by a clinical geriatrics team using our previously developed protocol Follow-up assessments All subjects were revaluated about delirium on each postoperative hospital day, and at 2, 4, and 6 weeks Ongoing adherence and safety monitoring	Intervention Initiate the study drug the day before surgery if possible, or within 24 hours after surgery. (Placebo appeared identical to donepezil) The study drug was administered daily, unless adverse events supervened, for a total treatment course of 30 days. 5 mg/ day dose of donepezil throughout the duration of the trial. After discharge, the remaining 30-day supply of "study drug" was sent with the patient for continued administration by the post- acute facility or by the family. Study coordinator contacted post-acute providers to ensure continuity of study drug treatment; also verified at follow up patient interviews <b>n = 9 placebo group</b> n = 2 withdrawals after discharge n = 1 withdrawal after week 4 Men and Women 4 (44%) Mean age 87.0 ± 3.7 Intervention: See above	Baseline characteristics Women Dementia ADL Score Primary outcomes Delirium Presence Hospital Interviews (more than one per subject) Week 2 Week 4 Week 6 Secondary outcomes Delirium Severity Hospital Discharge Week 2 Week 4 Week 6 Adherence Median % pills taken per days on protocol Delirium assessment: Baseline characteristics Primary outcomes Secondary outcomes	Donepezil vs Placebo No significant difference except gender 71% vs 44% 3 (43%) vs 4 (44%) NS $13.3 \pm 3.6$ vs $12.8 \pm 4.7$ NS No significant difference between groups 7/11 (64%) vs 9/14 (64%) p=0.9 3/7 (43%) vs 3/7 (43%) p=1.0 1/6 (17%) vs 3/7 (43%) p=0.6 3/6 (50%) vs 3/6 (50%) p=1.0 No significant difference between groups $1.3 \pm 2.5$ vs $1.6 \pm 5.2$ p=0.9 $-0.1 \pm 2.3$ vs $-2.2 \pm 4.9$ p=0.6 $-1.2 \pm 3.5$ vs $-2.0 \pm 6.4$ p=0.6 $-0.6 \pm 2.6$ vs $-2.0 \pm 7.5$ p=1.0 >90% both groups See above	Vomiting 1/7=14% vs 1/9=11% p=1.0 Syncope 1/7=14% vs 0/9 p=0. Dizziness 0/7 vs 1/9=11% p=1.0 Anorexia 0/7 vs 1/9=11% p=1. Frequency of Urination 1/7=14% vs 0/9 p=0.4 Total Side Effects per Patient Median (min, max) 2 (1, 3) vs (0, 3) p=0.02 Any Side Effects 7/7=100% vs 4/9=44% p=0.04 Serious Adverse Events Donepezil vs Placebo Total Number of Events Observed N=2 vs N=0 Number of Patients with SAE (%) 2/7=29% vs 0/9 p=0.2 Code Breaking Event: N=2 vs N=0 p=0.2 Drug Stopped Early N (%) 2 (29%) vs 3 (33%) p=1.0 Comments: This study has high ineligibility rates (nearly 2/3), and low enrollment rates (27%). The limitations are the small sample size and a very elderl population (average age in high 80's), which would be the population at greatest risk for delirium after hip fracture. The stratified randomization scheme achieved balance of pre-fracture dementia status.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
Balanced allocation (1 point if achieved):     Description of the method used for balanced allocation in sufficient detail to allow an     assessment of whether it should produce comparable groups. This will typically include     either a valid randomization procedure or prospective individual matching between     intervention and control groups.	0	Unclear	donepezil group had a higher proportion of women because of small sample
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	4/16 withdrawals during follow up
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	All patients analyzed (ITT not specified)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Total 16
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G2-Sampson EL, Raven PR, Ndhlovu PN, et al. A randomized, double-blind, placebo-controlled trial of donepezil hydrochloride (Aricept) for reducing the incidence of postoperative delirium after elective total hip replacement. Int J Geriatr Psychiatry. 2007;22(4):343-9.

Cturdy.	Denulation	Intervention Crows		Results	Adverse Effects
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Sampson EL 2007 UK Setting University hospital Study Design RCT (double blind, placebo controlled, parallel group) Randomization method block randomized by	N = 71 assessed for eligibility n = 21 excluded (see below) N = 50 randomized n = 14 Withdrawn after randomization n = 4 surgery canceled on medical grounds n = 10 withdrew consent N = 36 n = 3 loss of follow up N = 33 analyzed n = 19 donepezil	n = 21 Donepezil 5 mg n = 2 lost to follow up n = 19 analyzed Men and women (42.1%) Mean age 69.7 (8.4) MMSE 29.2 (1.4) Subjects received their first dose of study medication post- operatively upon return to the orthopedic ward following elective hip replacement, when they were able to tolerate sips	Delirium assessment: Delirium Symptom Interview (DSI) Baseline characteristics Primary outcomes incidence of delirium	DSI was rated by physicians or a trained research nurse in the morning of pre op and 3 times daily (morning, midday and evening) post op. Both incidence and severity measured by DSI with high interrater reliability No significant difference between groups 7 (21.2%) all patients <b>Donepezil vs placebo</b> 2 (9.5%) vs 5 (35.7%)	49 possible adverse events, bu none of these were considered to be serious and DPZ was we tolerated in this patient population. <b>Donepezil vs placebo</b> Nausea 6 vs 6 p=0.50 Vomiting 3 vs 1 p=0.45 Diarrhea 3 vs 2 p=0.90 Insomnia 9 vs 10 p= 0.16 Dizziness 4 vs 1 p=0.27 Paresthesia 1 vs 1 p= 0.82 Pyrexia 1 vs 1 p=0.82
he hospital pharmacy lepartment in groups of six (1:1 drug/ blacebo ratio) Study Length/Start- Stop Dates 0/2003 to 1/2004 days Purpose To assess nethodological	n = 14 placebo Inclusion Age >50 Elective total hip replacement surgery Attending the preadmission assessment clinic Informed consent Exclusion N = 21	of water. Subjects took 5mg of Donepezil or placebo every 24 h for 3 days. The total duration of treatment was 4 days. Pharmacy dispensed both DPZ and placebo throughout study; randomization codes remained concealed; all analysis done blind to randomization code	Relative risk (CI) Secondary outcomes Mean length of hospital stay (days) Difference in means Mean length of delirium (days) Difference in means	0.29 (0.06-1.30) 9.9 (0.73) vs 12.1 (1.09), p=0.09 -2.19 (-0.39 to 4.78) 1.5 vs 1.8 -0.3 (-0.38 to 1.41), p=0.83	Subjects with 1 AE: 1 vs 2 p= 0.37 Subjects with 2 AE : 17 vs 11 p= 0.38 Mean (SD) no. of AE per subject 1.84 (0.50) vs 1.71 (0.61) p=0.51 <b>Comments:</b> There was no evidence that DPZ was harmful; the drug wa well tolerated an no serious
easibility and the safety and efficacy of donepezil (DPZ) in preventing post- operative delirium after elective total hip eplacement surgery n older people without pre-existing	n = 17 refused to participate n = 4 withdrew consent MMSE <26 Sensory impairment Hypersensitivity to DPZ or piperidine derivatives Contraindications to DPZ	n = 15 placebo n = 1 lost to follow up n = 14 analyzed Men and women (57.1%) Mean age 65.1 (11.1) MMSE 28.8 (1.1) Placebo identical in	Delirium assessment: Baseline characteristics Primary outcomes Secondary outcomes	See above See above See above See above	adverse effects were reported. The results suggest possible benefits of DPZ over place with regard to the risk of delirium and length of hospital stay. The lack of significant benefit seen in this study may be due
dementia. Funding source(s): Educational grant from Pfizer Eisai, UK Quality Score 5 Risk of Bias: High		appearance to donepezil supplied by Pfizer Eisai UK			to the relatively good general health of this study population who had been selected as fit enough to undergo elective surgery. Methodological issues -small sample size -method of defining delirium may have increased sensitivity at the expense of specificity -not adequately powered to determine whether DPZ reduces delirium severity

**Conclusion**: The experimental paradigm was feasible and acceptable. Donepezil did not significantly reduce the incidence of delirium or length of hospital stay, however for both outcomes there was a consistent trend suggesting possible benefit.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Withdrawn after randomization =14 Loss of follow up = 3 Total dropouts = 17 (34%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Funding and placebo provide by Pfizer Eisai No ITT analysis
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Total sample: 36
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G2-Overshott R, Vernon M, Morris J, Burns A. Rivastigmine in the treatment of delirium in older people: a pilot study. Int Psychogeriatr. 2010;22(5):812-8.

<b>-</b> / ·	<b>_</b>		Resul		
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Overshott 2010	N = 15	n = 8 Rivastigmine group	Delirium assessment:	Daily rating (CAM) based on	A patient in the placebo group
JK	n = 2 withdrawn	n – 7 CAM negative for 3	CAM	MMSE by research nurse,	suffered from nausea.
		consecutive days		repeated by RA. Psychiatry	
Setting		n = 1 withdrew consent when CAM		determined if there was a	Three patients in the placebo
Academic hospital	Inclusion	negative for 2 consecutive days		difference. Inter-rater reliability	group needed additional
	Dx With delirium (CAM)			and delirium severity were not	psychotropic medication (either
Study Design	>65 yrs	Men: 4 (50%)		discussed.	risperidone or chlorrmethiazole
louble-blind, placebo-		Mean age 84.3 (11.2)			because of behavioral
controlled randomized	Exclusion	J J J J J J J J J J J J J J J J J J J	Baseline characteristics	Rivastigmine vs Placebo	disturbance.
oilot study	N = 69	Received rivastigmine 1.5 mg once		No difference between groups	
5	Renal disease= 20	a day increasing to 1.5 mg twice a		n = 8 vs 7	Comments
Randomization	Cardiac disease= 15	day after 7 days	Known dementia	3 vs 4, p = 0.62	
nethod	Too ill= 10		Mean MMSE (SD)at entry to trial	8.6 (4.9 ) vs 7.4 (7.1), p =0.7	The small number diagnosed
by numbered	Severe chest disease= 8		······································		with delirium may reflect that
reatment packets	Liver function tests= $6$		Primary outcomes		nurse informants who complete
statisticians.	Delirium resolved=3		Duration of delirium	6.3 (5.7 ) vs 9.9 (14.6 ), p=0.5	the CAM may have under-
	Refusal= 3		Duration of domain	0.0 (0.1 ) V0 0.0 (14.0 ), p=0.0	estimated the number and
Study Length/Start-	On a cholinesterase		Secondary outcomes		significance of symptoms of the
Stop Dates	inhibitor= 2		Number discharged	8 vs 3, p=0.03	patients, especially as the study
28 days	Transferred out of area= 1		Number CAM negative when left	0 vs 5, p=0.05	was conducted on busy acute
Lo days			study	8 vs 3, p=0.03	medical wards where the
Purpose	Alcohol detox= 1		Deaths during admission	0 vs 4, p=0.03	subtleties of the presentation of
To determine whether			Deaths during admission	0 vs 4, p=0.03	delirium (e.g. hypoalert delirium
ivastigmine would be		n = 7 slaasha ssaas	Delinium eccentrati	Cas shave	may not be identified because of
safe and helpful in the		n = 7 placebo group	Delirium assessment:	See above	
reatment of delirium.		n = 3 CAM negative for 3	Describes also as for visiting	0	high patient turnover and high
reatment of delirium.		consecutive days	Baseline characteristics	See above	workload.
/ `		n = 2 patients became too ill (both	<b>_</b> .		
unding source(s):		later died)	Primary outcomes	See above	The blinded researchers were
University Hospital of		n = 1 CAM positive for 28 days			very successful in identifying
South Manchester		(later died)	Secondary outcomes	See above	which patients were in which
NHS Foundation NHS		n = 1 withdrawn for protocol			treatment group.
Frust.		violation (medication			
		noncompliance)			This is unlikely to happen by
Quality Score					chance.
1		Men: 4 (57%)			
		Mean age 80.6 (8.5)			There was obviously some
Risk of Bias:		/			aspect of how patients
High		identical placebo administered as			progressed whilst in the trial
-		above (two tablets/day after 7			which suggested to researcher
		days)			which group the patient was in.
					3

**Conclusion**: The numbers of patients who screened positive for delirium was very small and as a result the sample size was too small to make any meaningful inferences about treatment of delirium. Despite the small numbers included in the study, there are some indicators that rivastigmine may be safe and effective in treating delirium.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	NOTE: see comments in regard to blinded researchers ability to identify group allocation
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Withdrawals: 2/15 (13%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	High	Did not report length of admission and discharge destination.
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Tablets were supplied by Novartis Pharmaceuticals U.K. Limited. No ITT analysis
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		T Total sample: 15
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G4-van Eijk MM, Roes KC, Honing ML, et al. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. Lancet. 2010;376(9755):1829-37.

<b>e</b> / 1				Results	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Van Eijk 2010	N = 648 had delirium	n = 55 Rivastigmine group	Delirium assessment:	Assessed daily by trained nurses with	The Data Safety and
Netherlands	n = 539 excluded (main	n = 1 withdrawn by family	CAM-ICU or CAM	CAM-ICU, and confirmed by research	Monitoring Board
	study)			nurse. Any doubts about the delirium	(DSMB) recommende
Setting	Study	n = 54 in ITT analysis	Delirium Severity Index (DSI)	diagnosis were resolved by a	that the trial be halted
Multicenter	N = 109 with delirium	n = 12 died	Definition Deventy mack (DOI)	psychiatrist, geriatrician, or neurologist	after the 4 <sup>th</sup> interim
6 ICUs	enrolled and randomized			consult. DSI for delirium severity.	analysis and inclusior
01005	enrolled and randomized	n 40 and of dolivium or discharge		consult. DSI for delinum seventy.	
	N = 404 is alread in ITT	n = 42 end of delirium or discharge	Descling characteristics	Divertionalist (54) we also be (50)	of 109 patients.
Study Design	N = 104 included in ITT	n = 6 died	Baseline characteristics	Rivastigmine (54) vs placebo (50)	<b>.</b>
RCT - double-blind,	analysis		No significant differences except		Mortality during
placebo-controlled	n=88 reached endpoint of	n = 36 completed follow up (90	Men	38 (70%) vs 29 (58%)	treatment with the
	end of delirium or	days)	Emergency admission	46 (85%) vs 32 (64%)	study drug seemed to
Randomization	discharge from hospital				be higher in the
method		Men: 38 (70%)	Primary outcomes	No significant differences	rivastigmine group
The trial pharmacist	n=75 completed 90 days	Mean age: 68.0 (11.4)	Delirium duration (days)	NS 5.0 (2.7–14.2) vs 3.0 (1.0–9.3) p=	n = 12 (22%) vs the
generated the	of follow-up	APACHE II score 20-3 (8-9)		0.06	placebo group n = 4
randomization		SOFA score 5.6 (2.3)	Endpoint of end of delirium (n=35	NS 4.0 (2.0–16.0) vs 2.5 (1.0–5.8)	(8%), p = 0.07 based
sequence (1:1) by	Inclusion	Charlson comorbidity index 2.6 (2.3)	vs n=34)	p=0.06	on sequential testing.
computer; stratified by	>18 yrs	2.3 (2.3)	Endpoint of hospital discharge	<b>NS</b> 6.0 (3.5–11.5) vs 6.0 (3.0–21.5), p=	
study center (all	admitted to ICU	Emergency admission to intensive	(n=7  vs  n=12)	0.95	The HR for delirium
investigators, patients	delirium (CAM-ICU)	care unit 46 (85%)	Endpoint of death	<b>NS</b> 9.5 (4.8–11.8) vs 8.0 (1.0–9.0) p=	duration associated
and families blinded)	stay in ICU > 48 h.	care unit 40 (0578)	(n=12 vs n=4)		with rivastigmine use
and families billided)	stay 11100 > 40 11.	Patients received an increasing	(11=12 VS 11=4)	0-29	
Church Law with (Chart	Fuchacian			Ciamificant differences and	was 0.72 (0.44-1,17)
Study Length/Start-	Exclusion	dose of rivastigmine or placebo,	Secondary outcomes	Significant differences only	did not change after
Stop Dates	N = 539	starting at 0.75 mL (1.5 mg	Median of mean DSI scores	2.3 (2,.0-3.1) vs 2,.0 (1.8-2.5) p 0.004	adjustment (0.77;
11/2008 to 1/ 2010	146 diagnosis uncertain	rivastigmine) twice daily and	Comatose (RASS -4 or -5)	69/659 (10%) vs 16/459 (3%) p <0.0001	0.47-1.26) or in post
	141 no informed consent	increasing in increments to 3 mL (6	Non-comatose (RASS -3 or	590/659 (90%) vs 443/459 (97%) p	hoc analysis 0.80
Purpose	65 renal replacement	mg rivastigmine) twice daily from	higher)	<0.0001	(0.51-1.14); and after
To establish the eff	therapy	day 10 onwards, as an adjunct to	ICU LOS	15 (9-30) vs 8 (3-17) p <0.0001	adjustment 0.84 (0.53
ect of the	22 hepatic encephalopathy	usual care based on haloperidol.			1.32) Post hoc
cholinesterase	15 unable to receive	n = 54 Placebo group	Delirium assessment:	See above	censored for discharg
inhibitor rivastigmine	enteric drugs	n = 4 withdrawn by family			from hospital but not
on the duration of	11 bradycardia	, , , , , , , , , , , , , , , , , , ,	Baseline characteristics	See above	death)
delirium in critically ill	139 other reasons	n = 50 in ITT analysis			,
patients.	31 could not speak Dutch	n = 4  died	Primary outcomes	See above	Mortality was evenly
Panonioi	or English		i initiary outcomes		balanced between
Funding source(s):	22 expected to be in	n = 46 end of delirium or discharge	Secondary outcomes	See above	participating centers.
ZonMw, the	intensive care	n = 7 died	Secondary outcomes	See above	participating centers.
Netherlands Brain	unit for <48 h				Protocol specified
		n = 20. completed fellow up (00			
Foundation, and	79 logistical problems	n = 39 completed follow up (90			analyses were not
Novartis	7 not specified	days)			done because the tria
					ended early so the
Quality Score	Evaluation after	Men: 29 (58%)			sample size was too
4	treatment:	Mean age: 70.0 (12.2)			small.
	Richmond agitation	APACHE II score 19.6 (7.9)			
Risk of Bias:	sedation scale (RASS)	SOFA score 5.5 (3.1)			Comments:
High	Sequential Organ Failure	Charlson comorbidity index 2.3 (2.3)			Rivastigmine was
-	Assessment	Emergency admission to intensive			associated with a mo
	(SOFA) scores	care unit 32 (64%)			severe type of
	, , , , , , , , , , , , , , , , , , , ,				delirium, longer stay i
		Identical placebo protocol (as			the ICU and higher
		above) (placebo drug same color,			mortality than placebo
		smell, taste and viscosity as			
		rivastigmine)			1

69

not support the use of cholinesterase inhibitors to treat delirium in critically ill patients

## In this trial, the cholinesterase inhibitor QUALITY / RISK OF BIAS RATING WORKSHEET

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant baseline differences between groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Early termination of trial due to deaths (also >10% dropouts)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	Unclear	Early termination of trial – follow up data not available
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Drug company sponsorship of study
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G4-Breitbart W, Marotta R, Platt MM, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. Am J Psychiatry. 1996;153(2):231-7.

Study	Population	Intervention Groups	Maggura	Results	Adverse Effects
Study Characteristics	Population	-	Measure	Outcome	Comments
Breitbart W 1996	N = 419 approached for	n = 11 haloperidol	Delirium assessment:	Trained research staff monitored study patients	No significant difference
USA	participation		DSM III R	daily for signs of delirium. Medical and nursing	-medical complications
	N = 244 informed consent	Treatment group-specific	Delirium Rating Scale	staff also trained. If delirium was suspected the	p<0.32
Setting		demographics not	MMSE	study coordinator and study psychiatrist	-severity of complication
Large metropolitan	N = 30 developed delirium	described		performed a full assessment	p<0.61
Cancer Center				Each study drug treatment protocol initiated	p toto i
	Men and women (23%)	Treatment protocol		(blinded); patients evaluated hourly with DRS,	Deaths (within 8 days of
Study Design	Mean age 39.2 (8.8) (23-56)	established for each study		MMSE and ESRS	protocol initiation)
RCT (double blind)	Mean age 55.2 (0.0) (25-50)	drug.			n = 2 haloperidol
	Inclusion	Dose level mg (1-9) for oral	Baseline characteristics	No significant difference between treatment	n = 2 chlorpromazine
Randomization	AIDS-related medical problems	and intramuscular	Dasenne characterístics	-	n = 1 lorazepam
	Medically stable	administration		groups	n = r iorazepani
method		auministration			Deathe within 4 weeks after
Hospital pharmacy	Informed consent (to delirium		Primary outcomes	Haloperidol vs chlorpromazine vs lorazepam	Deaths within 1 week afte
conducted	protocol if delirium developed)	Table 1, p 233 in PDF	Mean dose first 24 h (mg)	2.8 (2.4) vs50 (23.1) vs 3.0 (3,.6)	completing the protocol
randomization; also	Delirium present during study		Average maintenance dose	1.4 (1.2) vs 36.0 (18.4) vs 4.6 (4.7)	n = 3 chlorpromazine
identified study drug if	period				n = 1 lorazepam
significant adverse			Average DRS baseline	20.45 (3.45) vs 20.62 (3.88) vs 18.33 (2.58)	
effects occurred	Exclusion		Average DRS day 2	12.45 (5.87) vs 12.08 (6.50) vs 17.33 (4,18)	Extrapyramidal side
	N = 175 (no specific data)		Average DRS end of tx	11.64 (6.10) vs 11.85 (6.74) vs 17.00 (4.98)	effects = none
Study Length/Start-	Hypersensitivity to neuroleptics		Main effect for time	F = 10.09, df=2,27, p<0.001	-no effect for time,
Stop Dates	Hypersensitivity to			Main effect for drug NS (p<0.44)	p<0.81
28 weeks	benzodiazepines		Significant decrease in DRS		-drug by time interaction
	Presence of neuroleptic		Baseline to day 2	F = 27.50, df=1, 27, p<0.001	= trend, p<0.07
Purpose	malignant syndrome		No significant difference in		-increase in lorazepam
To determine the	Concurrent treatment with		DRS day 2 to end of tx	P<0.43 vs p<0.81 vs p<0.81	group
safest and most	neuroleptic drugs		5		0
effective	Seizure disorder	n = 13 chlorpromazine	Delirium assessment:	See above	Comments
pharmacotherapies	Current systemic chemo-				
for the management	therapy	Treatment protocol – see	Primary outcomes		This study confirmed the
of the mental	Withdrawal syndrome	above	Significant decrease in DRS		clinical efficacy of
symptoms and	Anticholinergic delirium	Table 1, p 233 in PDF	Baseline to day 2	F=37.02, df=1, 27, p<0.001	neuroleptic drugs in the
behavioral	Current or past dx	10010 1, p 200 in 1 D1	Baseline to day 2	MMSE improved only for chlorpromazine group	amelioration of delirium
disturbances	-schizophrenia		MMSE baseline to day 2	F=13.99, df=1,27, p<0.001	symptoms in AIDS
associated with	-schizoaffective disorder		MMSE baseline to end of tx	F=4.68, df=1,27, p<0.04	patients.
delirium in AIDs	-bipolar disorder			1 =4.00, di=1,27, p<0.04	patients.
	Participation would				In addition, lorazepam
patients.	compromise obtaining needed	n = 6 lorazepam	Delirium assessment	See above	alone is not effective in the
Funding source(s):	medical treatment	II – O IOIazepaili	Deminum assessment		treatment of delirium in
Not described	Delirium associated with	Treatment protocol – see	Primary outcomes		AIDS patients,
Not described		above	No significant decrease in		AIDS patients,
	terminal event			$E_{-0.22}$ df 1.27 p = 0.62	The decase of neutrolantice
Quality Score	Lacked capacity for informed	Table 1, p 233 in PDF	DRS Baseline to day 2	F=0.23, df=1,27, p<0.63	The doses of neuroleptics
3	consent		The star set l'address it i		required to manage
			Treatment-limiting side	All 6 patients developed side effects	delirium in AIDS patients
Risk of Bias:	Assessments		effects	-increased confusion	may be considerably lowe
Unclear	Delirium Rating Scale (DRS)			-oversedation	than many reported in
	DSM III R			-disinhibition	clinical standards.
	MMSE (also used to guide			-ataxia	
	ratings on delirium severity)			Lorazepam treatment discontinued	There may be disease
	Extrapyramidal Symptom				specific mechanisms that
	Rating Scale (ESRS)			Subsequent patients randomized to haloperidol	explain why patients with
	Side Effects and Symptoms			or chlorpromazine	AIDS required low doses.
		1	1		
	Checklist				
	Montol Status Brafila			fects by using low-dose neuroleptics (haloperidol or	

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Unclear	Baseline date not reported except for age and gender of 30 patients with delirium
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not clear whether outcome assessors were blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Total patients approached and number consented, but no specific data on exclusions
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	All patients analyzed, but ITT protocol not performed Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on <u>the criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

# G2-Marcantonio ER, Juarez G, Goldman L, et al. The relationship of postoperative delirium with psychoactive medications. JAMA 1994;272(19):1518-1522.

_				Results	_
Study Characteristics	Population	Study Groups	Measure	Outcome	Comments
Marcantonio ER 1994	N = 1341 in prospective	n = 91 developed delirium	Delirium assessment:	Delirium dx by meeting criteria on ≥1 day	Medication exposure
USA	cohort	during post op days 2-5	CAM	after the first postop day. CAM	(all patients)
	N = 245 delirium +no delirium		MEDICUS	administered daily by trained study	Narcotics = 94%
Setting	n = 91 delirium	Men and women (50%)		personnel post op days 2-5. In addition,	Benzodiazepines = 139
Jniversity Hospital	n = 154 no delirium	Mean age 73 (8)		altered mental status in both the medical	Anticholinergics = 9%
General, Orthopedic		3 - (-)		record and in MEDICUS on the same day	5
and Gynecologic	Inclusion	Daily structured interviews by			There was no
Surgery Depts)	Age >50	study personnel (days 2-5	Baseline characteristics	No significant differences between groups	interaction between the
burgery Depts)	Major elective non-cardiac	postop; or day before		in preoperative risk factors	associations of drug
Study Decian	procedures		Primary outcomes		exposure with delirium
Study Design		discharge if before 6 days)		Delinium us ne delinium	
Prospective cohort	Hospital stay ≥2 days	-designed to test orientation	(matched analysis)	Delirium vs no delirium	and the preoperative
nested case control		and attention		Differences between groups	delirium risk scores.
	Exclusion	Mental status based on		% vs %, OR (CI) (risk for delirium)	
Selection method	N =	medical record (MEDICUS	Narcotics (class)	95% vs 94%; 1.4 (0.5-4.3)	Postoperative
Cases and controls	Not described	instrument)	Meperidine	65% vs 42%; 2.7 (1.3-5.5)	exposures to
derived from a			Morphine	24% vs 34%; 1.2 (0.6-2.4)	meperidine and
prospective cohort study	Preoperative evaluation	Medication exposures recorded	Fentanyl	10% vs 9%; 1.5 (0.6-4.2)	benzodiazepines were
of patients consenting to	-medical hx review	for the 24 h before delirium	Oxycodone	10% vs 19%; 0.7 (0.3-1.6)	independently
preoperative evaluation	-physical exam	developed	Codeine	7% vs 7%; 1.1 (0.4-3.6)	associated with the
	-functional status testing		Epidural administration	64% vs 42%; 2.3 (1.2-4.4)	development of deliriur
Study Length/Start-	-cognitive status testing		Meperidine (epidural)	57% vs 34%; 2.4 (1.3-4.4)	within the next 24
Stop Dates	-laboratory tests		Fentanyl (epidural)	5% vs 8%; 0.9 (0.3-2.7)	hours.
11/1990-3/2002			Patient controlled	370 V3 870, 0.5 (0.5-2.7)	nours.
11/1990-3/2002	Testing instruments		administration	22% vs 32%; 1.1 (0.5-2.2)	Although epidural
Purpose	Specific Activity Scale		Meperidine (PCA)	4% vs 3%; 2.1 (0.4-10.7)	analgesia was
To determine whether	Telephone Interview for		Morphine (PCA)	18% vs 29%; 0.9 (0.4-1.9)	associated with
post-operative	Cognitive Status (TICS)			NOTE: p value not provided for narcotics	delirium, it appears the
exposures to certain					association may be
medications were	Medication classes studied		Benzodiazepines (class	21% vs 8%; 3.0 (1.3-6.8), p <.01	related to the use of
ndependently	Narcotics		Long acting	7% vs 2%; 5.4 (1.0-29.2) Long vs short	meperidine in 85% of
associated with delirium,	Benzodiazepines		Short acting	14% vs 6%; 2.6 (1.1-6.5)  p = .02	patients receiving
after controlling for pre-	Anticholinergics		High Dose	11% vs 3%; 3.3 (1.0-11.0) High vs low	epidural analgesia.
operative risk	-		Low dose	10% vs 5%; 2.6 (0.8-9.1) p = .03	
	Preoperative Risk Factors				The matched design of
Funding source(s):	independently associated		Anticholinergics (class)	11% vs 8%; 1.5 (0.6-3.4), NS	this study controlled for
Grant funding	with postoperative delirium		Diphenhydramine	10% vs 6%; 1.8 (0.7-4.5), NS	confounding by known
-Agency for Health	(for matching controls)		High dose	3% vs 3%; 1.5 (0.3-6.9), NS high vs low	preoperative risk factor
Care Policy and	Age		Low dose	8%  vs  5%; 1.5 (0.5-4.1),  NS $p = .66  NS$	for delirium and by
Research	Poor cognitive function	n = 154 no delirium (controls)	Eow dosc	0.00000 = 0.000000000000000000000000000	studying only surgical
-National Research	Poor physical function	1 or 2 selected controls who	Delirium assessment:	See above	patients, although
	Self-reported alcohol abuse		Dennum assessment:	See above	
Service Award for	•	did not have delirium matched	Describes also as desired as	On a share	neither of these
Research in Primary	Abnormal preop serum	for each case based on the	Baseline characteristics	See above	eliminates all potential
Care Medicine	-sodium	same preoperative risk for			confounding .
-Established	-potassium	delirium (if >2 patients	Primary outcomes	See above	
Investigator Award	-glucose	matched, 2 randomly selected)			By limiting the exposure
(AHA)	Aortic aneurism surgery		Secondary outcomes	See above	window to the 24-hour
	Noncardiac thoracic surgery	Men and women (50%)	-		period before delirium
Quality Score		Mean age 73 (8)			developed, this study
5		<b>č</b> ( <i>i</i> ,			tried to eliminate
		Daily structured interviews (see			medication exposures
Risk of Bias:		above)			given in response to
Unclear		Medication exposure (see			delirium.
		medication exposure (see	1		aointuitt.
Cholodi		above			

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – case control design
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	NA – case control design
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Possible confounders (despite attempts to control for them)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

# G4-Pisani MA, Murphy TE, Araujo KL,,et al. Benzodiazepine and opioid use and the duration of intensive care unit delirium in an older population. Crit Care Med. 2009;37(1):177-83.

Study	Population	Intervention	Results		Adverse Effects
Characteristics	•		Measure	Outcome	Comments
Pisani 2009 USA	N = 725 screened n = 318 eligible	Other assessment: short form of the Informant	Delirium assessment: Confusion Assessment Method-ICU	Trained research nurses rated CAM-ICU based on	Adverse Effects were not discussed.
	n = 309 enrolled	Questionnaire on Cognitive	(CAM-ICU)	cog test Monday through	
Setting	n = 5 excluded due to	Decline in the Elderly (IQCDE)		Friday. Inter-rater reliability	Comments
Intensive care unit in	persistent stupor or coma			was 100%	The author did not examine
an urban university	Study N = 304	Katz Activities of Daily Living		CAM ICU supplemented by	benzodiazepines and opioids
teaching hospital.		Scale (ADL)		daily validated chart review	separately because only 28
todorinig ricopitali	Men (%) 143 (47%)			method	participants received a
Study Design	Mean age 75 (8)	Lawton's Instrumental Activities	Baseline characteristics		benzodiazepine exclusively,
Prospective cohort		of Daily Living	ICU delirium data	N = 304	32 received an opioid
study	Dementia: 94 (31%)	Scale (IADL)	Patients with delirium	239 (79%)	exclusively, and all 21
,	Hx depression 85 (28%)		Dementia and delirium	89 (37%)	receiving propofol also
Selection method	Alcohol use: 120 (40%)	Charlson Comorbidity	Patients with dementia, delirium and		received a benzodiazepine
Consecutive	ADL disability: 110 (36%)	Index	agitation	26 (29%)	and opioid.
admissions to medical	IADL disability: 260 (86%)		No dementia and delirium	148 (62%)	
ICU	Charlson Index: 1.8 (1.9)	Acute Physiology and Chronic	No dementia, delirium and agitation	57 (38%)	The author reviewed receipt of
	Benzodiazepines or opioids	Health Evaluation Status score	First episode of ICU delirium (days,		haloperidol and sedation
Study Length/Start-	on admission: 75 (25%)	(APCHE II)	mean (SD)	4.7 (5.8)	status in the cohort and found
Stop Dates	Full code status on ICU		First episode of ICU delirium (days,		that the majority of patients
9/5/ 2002 - 9/30/2004	admission 260 (86%)		median, range)	3 (1-33)	had delirium and 70% had
_	Body mass index: 25.8	Drug data for the study	Delirium on day of ICU discharge	83 (27%)	agitation on the first day they
Purpose		population (n=304)			received haloperidol.
To examine the impact	Inclusion	Benzodiazepine or opioid use:	Bivariate analysis for delirium	N=304 RR (LR), p	
of benzodiazepine or	>60 yrs	247 (81%	duration outcome:	(significant results)	However, the author does not
opioid use on the	admitted to ICU	) Marilian ta hinkarata any	Benzodiazepine or opioid use	1.89 (31.49) p<0.001	have documentation on what
duration of ICU	Fuchasian	Medium to high potency	Haloperidol use	1.42 (43.71) p<0.001	prompted prescription of
delirium in an older	Exclusion N = 416	anticholinergic medication use:	Impairment in ADL	1.15 (6.40) p=0.01	haloperidol to the patients.
medical population.	193 admission <24 hr	98 (32%)	History of depression Dementia (IQCDE)	1.15 (6.04) p=0.01 1.21 (11.24) p<0.001	The major innovation of the
Funding source(s):	83 transfer from another ICU	Haloperidol use at any point	APACHE II minus Glasgow	1.01 (4.76) p = 0.03	study is its examination of
CG-002-N,	52 inability to communicate	during the ICU stay:97 (32%)	Intubated	1.81 (67.34) p<0.001	duration of delirium rather than
P30AG21342	before admission		Restraint use	1.94 ( 95.22) p<0.001	occurrence.
NIH K23 (K23 AG	56 no identifiable proxy	Steroid use at any point during		1.04 ( 00.22) p<0.001	
23023-01A1).	23 non-English speaking	the ICU stay: 158 (52%)	Multivariable models for delirium	N = 304 RR (CI), p	This is advantageous in an
#R21AG025193 ,	8 proxy refusals		duration	(significant results)	ICU study because so many
#K24AG000949 from	1 patient refusal.		Benzodiazepine or opioid use <sup>1</sup>	1.64 (1.27–2.10), p <0.001	patients have delirium on the
NIA			Control for dementia	1.19 (1.07-1.33), p = 0.002	first day of their ICU stay.
	Data sources		Control for haloperidol	1.35 (1.21-1.50), p <0.001	, ,
Quality Score	Proxy interviews		Control for APACHEII minus Glasgow	1.01 (1.00-1.02) p = 0.02	A second strength is the firm
5	Medical records		Effect of benzodiazepines or opioids		establishment of a temporal
	Prospective data collection		when dementia is absent <sup>2</sup>	2.42 (1.65–3.55), p <0.001	ordering between receipt of
Risk of Bias:	after admission to ICU		Effect of haloperidol when dementia is		medications and delirium to
High			absent <sup>3</sup>	1.47 (1.29–1.69), p <0.001	ensure their receipt before or
					concomitant with the first
			1: controlling for dementia, use of		episode of delirium.
			haloperidol, and baseline health status		
			2: Controlling for use of haloperidol and		
			baseline health status		
			3. Controlling for use of opioids or		
			benzodiazepines and baseline health		
			status		
					<u> </u>

**Conclusion:** The use of benzodiazepines or opioids in the ICU is associated with longer duration of a first episode of delirium. Receipt of these medications may represent modifiable risk factors for delirium. Clinicians caring for ICU patients should carefully evaluate the need for benzodiazepines, opioids, and haloperidol.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Observational study (one group)
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observational study (one group)
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observational study (one group)
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low risk of bias:

   o
   Unclear risk of bias:
   High or unclear risk of bias on 1 or more of 6 domains

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  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4-Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology. 2006;104(1):21-6.

Study	Population	Study Components	Re	sults	Adverse Effects
Characteristics			Measure	Outcome	Comments
Pandharipande P	N = 275 consecutive patients	Sedative and analgesic	Delirium assessment:	Daily assessment using RASS	Adverse effects not discussed
2006	n = 77 excluded (see below)	medications prescribed	CAM-ICU	and CAM-ICU (no detailed	
	N = 198 analyzed	according to a protocol	RASS	description)	Comments
JSA	n = 696 observations	adapted from the guidelines	10.00	description)	oonmento
	11 - 090 00361 Valions	of the Society of Critical	Baseline characteristics	Single group; no comparison	Every unit dose of lorazepan
Setting	Max and (400()		Baseline characteristics	Single group; no comparison	
Jniversity Medical	Men and women (48%)	Care Medicine		NL 400	was associated with a higher
Center	Mean age 55.5 (17.0)		Primary outcomes	N = 198	risk of transitioning into
	Charlson Comorbidity Index 3.6 (2.8)	Medications titrated by	Total observations	696 included in analysis	delirium each subsequent 24
Study Design	Vision deficits 114 (56%)	bedside nurses to achieve			hour period even after
Prospective cohort	Hearing deficits 32 (16%)	<ul> <li>a target sedation level</li> </ul>	Risk for transitioning to	Multivariate analysis	adjusting for 11 relevant
	Dementia score 0.2 (0.7)	determined by the treating	delirium	OR (CI), p	covariates.
Selection method	ADLs 0.9 (2.3)	time using RASS	Lorazepam	1.2 (1.1-1.4), 0.003	
Consecutive patients	APACHE II 25.7 (8.4)	-pain level using a	Midazolam	1.7 (0.9-3.2), 0.09	The use of opiates and
	SOFA 10.0 (3.3)	behavioral pain indicator	Fentanyl	1.2 (1.0-1.5), 0.09	sedatives (for the "double
neeting inclusion	Admission dx (>11%)	scale developed by the	Morphine	1.1 (0.9-1.2), 0.24	effect") which reduces the
criteria	-Sepsis/ARDS 47%	medical ICU	Propofol	1.2 (0.9-1.7), 0.18	need for benzodiazepines or
	-Pneumonia 19%	incucal 100	Тюрыы	1.2 (0.0-1.7), 0.10	propofol may be prudent.
Study Length/Start-	-Other 29%	Analganian		Incremental dage beyond 20 mg	proportion may be proderit.
Stop Dates	-Other 29%	Analgesics	Lorazepam dose	Incremental dose beyond 20 mg	
2/2000 – 5/2001		-morphine	(Fig 1)	lorazepam in the preceding 24 h	Considering that delirium is a
	Inclusion	-fentanlyl		= 100% probability of	predictor of death and other
Purpose	Any adult	Sedatives		transitioning to delirium (p =	adverse outcomes,
To study the temporal	Mechanically ventilated	-lorazepam		0.003)	investigators should conside
elation between time	Admission to medical or coronary ICU	-propofol	Drug-drug interaction		prospective interventional
of administration of	Informed consent from patient or	-midazolam	(lorazepam + each drug)	None (all p values >0.05)	studies to determine whether
sedatives/analgesics	surrogate				differing management
and development of		Risk factors	Previous cognitive status	None (did not modify	strategies or selection of
delirium and	Exclusion	-age	5	contributory risk of these	sedative/analgesic agents are
	N = 77	-visual and hearing deficits		medications in transitioning to	associated with reductions in
differentiate whether	51 = persistent coma	-history of dementia		delirium)	delirium and other short- and
sedatives/analgesics	26 = lack of 2 consecutive cognitive	-depression (GDS)			long-term clinical outcomes.
were administered to	assessments	-severity of illness	Age >65	Probability increased for each	long term ennear outcomes.
reat the delirium or	233635116113	(modified APACHE II –	(Fig 2)	year of life after 65 ( $p = 0.004$ )	Limitations
whether exposure to	NOTE datailed departmention of		(Fig 2)		
hese agents resulted	NOTE detailed description of	removing the Glasgow		OR 1.02 (1.00-1.03), p = 0.04)	-the list of covariates was no
n delirium.	Inclusion/Exclusion provided in	Coma Scale)	Interaction lorazepam/age	None	all-inclusive; excluding
	previous papers (Ely et al 2001;	-sepsis			-renal/hepatic dysfunction
Funding source(s):	Milbrandt et al 2004; Ely et al 2004;	-history of neurologic	APACHE II	Probability increases for each	-hypoxemia
Not described	Ely et al 2003; See references #8, 9,	disease	(Fig 3)	additional point up to 18 then	-sleep deprivation
	14, 15)	-baseline hematocrit		plateaus (0.004)	-more frequent delirium
Quality Score		<ul> <li>-daily serum glucose</li> </ul>		OR 1.06 (1.02-1.11), p = 0.004	assessments would have
3	Assessments	concentrations			allowed better tracking of
	Richmond Agitation Sedation Scale		Antipsychotic exposure	Administered to 75/198 (38%)	cognitive status
Risk of Bias:	(RASS)		Delirium incidence	66/75 (88%)	-used administered drug
	Geriatric Depression Scale (GDS)			Not associated with transition to	dose rather than plasma
High	Blessed Dementia Rating Scale			delirium ( $p = 0.39$ )	concentrations
	(dementia score)			(P 0.00)	-excluded observations
	Katz Activities of Daily Living (ADLs)		Anticholinergic exposure	Administered to 63/198 (32%)	without accompanying asses
			Delirium incidence		
	Acute Physiology and Chronic Health			52/63 (83%)	ments
	Evaluation II (APACHE II)			Not associated with transition to	-only cursory evaluations of
	Sequential Organ Failure Assessment			delirium (p = 0.82)	antipsychotics and
	(SOFA				anticholinergics

**Conclusion:** This study (using Markov regression modeling) documented that in addition to advancing age and APACHE II scores, there is an independent and dose-related temporal association between receiving lorazepam and transitioning to delirium, even after adjusting for relevant covariates.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
Balanced allocation (1 point if achieved):     Description of the method used for balanced allocation in sufficient detail to allow an     assessment of whether it should produce comparable groups. This will typically include     either a valid randomization procedure or prospective individual matching between     intervention and control groups.	0	High	Single group (no comparison)
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – single group
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA – single group
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Observations excluded if no associated assessment(s) ?%
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Although multivariate analysis, limitations note possible confounding variables Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
<ul> <li>8. Sample size ≥50 each study arm (1 point if achieved):</li> </ul>	1		
o. Sample size ≥ou each study arm (1 point ir achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low risk of bias:

   o
   Unclear risk of bias:
   High or unclear risk of bias on 1 or more of 6 domains

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  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4- Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. Anesthesiology. 2012;116(5):987-97.

				ults	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Hakim 2012	N = 101	n = 51 risperidone 0.5 mg q12h	Delirium assessment:	If ICDSC >3, psychiatrist	Risperidone vs Placebo
Egypt	n = 51 intervention	po.	Statistical Manual of Mental	confirmed delirium using DSM	Extrapyramidal:
	n = 50	-	Disorders (DSM)	criteria	2 (3.9%) vs 1 (2%); P=1.0
Setting	Inclusion	Men/women = 33/18		no inter-rater reliability, no	Death:
University hospital	>65 yr	Age: 65 to 70 yr 36 (70.6%)		cognitive testing done, no other	2 (3.9%) vs 1 (2%)
	Undergoing on-pump cardiac	>70 yr 15 (29.4%)		details described.	Mechanical ventilation:
Study Design	surgery	Intervention	SSD assessment:	See population column	3 (5.9%) vs 2 (4%)
A randomized,	No history of neuropsychiatric	The test drugs were continued for			Second operation:
double-blind, placebo-	disorders, alcoholism,	24 h after subsidence of SSD (0 on	Provide baseline		1 (1.96%) vs 2 (4%)
controlled, parallel-	substance abuse, or intake of	the ICDSC) or until ICDSC >3.	zharacteristics/measures	Risperidone vs Placebo	Abnormality of the QTc
arm study	psychotropic medications.	Patients who experienced delirium,	Demographic and Pre-op Data	No significant difference	interval and emergency
·	With SSD (ICDSC 1-3)	the dose of risperidone was	- MMSE score (28-30)	30 (58.8%) vs 31 (62%)	breaking of the
Randomization		incrementally increased until	- MMSE score (25-27)	21 (41.2%) vs 19 (38%)	concealment envelopes
method	Exclusion	symptoms were controlled or	-GDS (0-2)	25 (49%) vs 26 (52%)	0 vs 0
Randomization was	N= 142	attained dose of 4 mg/d.	-GDS (3-4)	26 (51%) vs 24 (48%)	
carried out by a	19 Declined to participate	Ģ	Operative and Post-op Data	No significant difference	Comments:
clinical pharmacist	47 Not meeting inclusion criteria	n = 50 placebo q12h po.	-post-op intubation >24 h	5 (9.8%) vs 3 (6%)	The current study showed
using a computer-	76 Not meeting criteria for SSD		ICDSC score 1	19 (37.3%) vs 17 (34%)	that 57.1% of patients
generated random	Exclusion criteria:	Men/women = 36/14	ICDSC score 2	17 (33.3%) vs 17 (34%)	experienced SSD after
number list created	MMSE<25	Age: 65 to 70 yr 39 (78%)	ICDSC score 3	15 (29.4%) vs 16 (32%)	surgery. The incidence of
with GraphPad	GDS >4	>70 yr 11 (22%)			clinical delirium observed
StatMate v.1.01i	Impaired hearing or visual acuity		Primary outcomes:		in the current study was
software using	Speech difficulty	Intervention (see above)	Possibly delirious: ICDSC >3	8 (15.7%) vs 19 (38%), p =.011	23.8%.
permuted blocks of	Contraindication to risperidone	Patients in the placebo group who	Incidence of delirium (DSM)	7 (13.7%) vs 17 (34%), p =.031	
size 4.	or haloperidol	experienced delirium were given	Absolute risk reduction	0.20 (95% CI, 0.04 – 0.37)	Neither the ICDSC nor the
Study Length/Start-	Hx of neuroleptic malignant	0.5 mg oral risperidone every 12 h,	Number needed to treat	4.9 (95% CI, 2.7–24.4)	CAM-ICU has been
Stop Dates	syndrome,	and if symptoms were not			validated for severity
12/2007 – 11/2010	Prolonged QTc syndrome	controlled, the dose could be	Secondary outcomes:		scoring of delirium, so the
	Hx cerebrovascular disease	increased to 4 mg/d.	Duration of delirium	3 (2 to 4) vs 3 (3 to 4) p=.664	highest score on the
Purpose	other noncardiac procedures	5	Need for haloperidol	2 (28.6%) vs 3 (17.6%) p=.608	ICDSC was reported in the
To evaluate the effect		In either group, haloperidol was	Highest doses of risperidone	3 (2 to 4) vs 3 (2.25 to 3.5) p=.318	current study as a
of treating	Assessment of SSD:	used as a second line rescue	Highest doses haloperidol	0 (0 to 1.5) vs 0 (0 to 0) p=.757	measure of severity,
subsyndromal	Screening SSD using the	medication if symptoms were not	Highest score on the ICDSC	6 (5 to 7) vs 5 (4 to 5) p=.234	taking advantage of the
delirium (SSD) with	Intensive Care Delirium	controlled with risperidone in a	Length of ICU	2 (2 to 3) vs 3 (2 to 3) p=.517	ordinal framework of this
risperidone on the	Screening Checklist (ICDSC):	daily dose of 4 mg.	LOS	6 (5 to 7) vs 6 (5 to 8) p=.056	scale.
incidence of clinical	physician who were trained		Extrapyramidal side effects	2 (3.9%) vs 1 (2%) p=1.0	
delirium in elderly	systematically assessed 4 h	Haloperidol was begun orally at 0.5			it is probable that the
patients who	after extubation and each 8-h	mg q8h and could be escalated to	Adjusted analysis:		study had low power to
underwent on-pump	nursing shift. Define SSD as	10 mg/d if needed. Rescue	Failure to treat SSD with	3.83 (95% CI, 1.63– 8.98; P=.002)	detect a statistically
cardiac surgery.	ICDSC score of 1-3.	medications were started once the	risperidone		significant difference
0, 1		diagnosis of delirium was	Rudolph Risk Score	2.62 (95% CI, 1.51–4.53; P=.001)	between the two groups
Funding source(s):	All patients protocol:	confirmed, and the dosage could		/	with regard to ICU,
Support was provided	standardized balanced	be escalated by doubling the dose			hospital length of stay,
solely from	anesthetic technique,	at 24-h intervals, if needed, until			duration of delirium,
institutional and/or	cardiopulmonary bypass, and a	symptoms were controlled or the			highest score on the
departmental sources.	standard protocol was	maximum dosage limit was			ICDSC, or consumption of
• • • • • • • • • •	implemented for sedation,	attained.			antipsychotic medications.
Quality Score = 8	analgesia, and management of				
Risk of Bias: Low	mechanical ventilation after	Rescue medications were			
	surgery (see PDF).	continued for 24h after a score of 0			
	<b>G y (- - - )</b>	was achieved on the ICDSC.			
Conclusion: Using risp	eridone in elderly patients who expe	rienced subsyndromal delirium after or	pump cardiac surgerv was associated	with significantly lower incidence of d	elirium.

#### RATING WORKSHEET

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	Based on the intention to treat.
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = Low
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 8

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4-Girard TD, Pandharipande PP, Carson SS, et al. .Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. Crit Care Med. 2010;38(2):428-37.

Study	Population	Intervention Groups		Results	Adverse Effects
Characteristics	Fopulation	_	Measure	Outcome	Auverse Ellects
Girard 2010	N = 103 randomized and	n =35 haloperidol every 6	Delirium assessment:	CAM-ICU rated by trained RAs twice	Haloperidol vs
JSA	analyzed	hrs x 14 days	Confusion Assessment	daily based on RÁSS.	ziprasidone vs
	n = 35 haloperidol	n = 2 discontinued protocol	Method for the ICU (CAM-ICU)	Inter-rater reliability was not discussed.	Placebo
Setting	n = 30 ziprasidone	n = 2 withdrew	RASS	, , , , , , , , , , , , , , , , , , , ,	Akathisia:
Aulticenter – 6 tertiary	n = 36 placebo	n = 35 analyzed			10 (29%) vs 6 (20%) v
care medical centers				Haloperidol vs ziprasidone vs Placebo	7 (19%) (p =0 .60)
		Female, 15 (43%)	Baseline measures	No significant difference between groups	r (10,0) (p =0.00)
Study Design	Inclusion	Mean age 51 (35–59)	APACHE II score	26 vs 26 vs 26	Extrapyramidal
Randomized, double-	>18 yrs	Mean age 51 (55–59)	Brain dysfunction	20 13 20 13 20	symptoms
blind, placebo-controlled	ICU patients had abnormal level of	5 mg haloperidol (as a	-Delirium	16 vs 15 vs 17	similar between
rial.	consciousness or were receiving	solution containing 1	-Coma	12 vs 9 vs 14	
inai.			Haloperidol before enrollment	1 vs 2 vs 4	treatment groups (p
Developminetien weethed	sedative or analgesic medications	mg/mL)			=0.46).
Randomization method	Freeheelen		Ziprasidone before enrollment	0 vs 0 vs 0	<b>O</b>
Computer-generated,	Exclusion	n = 30 ziprasidone every 6	Delesson	Helen eridelen einerstelen ein Blackha	Comments:
permuted block	N =3194	hrs x 14 days	Primary outcomes	Haloperidol vs ziprasidone vs Placebo	
randomization scheme	1000 neurologic injury	n = 0 discontinued/ withdrew		14.0 (6.0–18.0) vs 15.0 (9.1–18.0) vs	This pilot study was
stratified according to	536 high risk of VT	n = 30 analyzed	Delirium/coma-free days	12.5 (1.2–17.2)	designed primarily to
study center.	344 ventilated >60 hrs				demonstrate the
	190 had no gastric access	Female, 9 (30%)			feasibility of a double-
Study Length/Start-	174 post-suicide attempt	Mean age 54 (47–66)	Secondary outcomes		blind, placebo controll
Stop Dates	108 used neuroleptics		ventilator-free days hospital	7.8 (0–15.0) vs 12.0 (0–18.6) vs 12.5 (0–	trial of antipsychotics
21-day study period	107 severe dementia	40 mg ziprasidone (as a		23.3) (p =0.25),	ICU delirium, it was
2/2005 – 7/2007	44 post-liver transplant	solution containing 8			likely significantly
	19 pregnant	mg/mL)	length of stay	13.8 vs 13.5 vs 15.4 (p =0.68)	underpowered to
Purpose	16 neuroleptic allergy	<b>3</b>			demonstrate the
To demonstrate the	247 enrolled in other study		21-day mortality	4 vs 4 vs 6 (p = 0.81).	potential efficacy for
feasibility of a placebo-	210 no informed consent	n =36 placebo every 6 hrs		u ,	many outcomes
controlled trial of		x 14 days	Average extrapyramidal		including length of stay
antipsychotics for	All patients protocol:	n = 2 discontinued	symptoms score	0 (0–0.2) vs 0 (0–0) vs 0 (0–0) p=0.56	and survival.
delirium in the intensive	• •	n = 1 withdrew	, , , , , , , , , , , , , , , , , , , ,		
care unit and to test the	The second dose of study drug	n = 1 received EoL care		Haloperidol vs ziprasidone (OR (CI), p)	Limitations of the trial
hypothesis that	was administered 12 hrs after if	n = 36 analyzed	Daily delirium risk	1.2 ( 0.6 –2.2) vs 1.1 ( 0.5–2.2),p= 0.80	include the small
antipsychotics would	QTc interval >500 msec; and then	n – oo anaryzea	,	··· ( •·• -·· ( •·• -·· ( •·• -·· ),p • •·••	sample size, lack of
improve days alive	g6h.	Female, 14 (39%)	Study drug delivery and other	No significant difference	enforcement by study
without delirium or coma.	9011	Mean age 56 (43–68)	antipsychotics		personnel of a
without definition of conta.	Study drug frequency was reduced	Mean age 50 (45-00)	anapoyonolioo		standardized sedation
Funding source(s):	to every 8 hrs when patients were	pleases (as a 5 ml solution)			protocol, and the
NIH HL007123, the	two consecutive negative for CAM-	placebo (as a 5-mL solution)			exposure of some
Hartford Geriatrics	ICU.				patients in the
Health Outcomes	160.				ziprasidone and
Research Scholars	Reduced to every 12 hrs when				placebo groups to ope
Award Program, the	patients were delirium/coma-free				label haloperidol.
Award Program, the Vanderbilt Physician	on three consecutive				
Scientist development	assessments, and discontinued				
Program, and GRECC.	when patients were delirium/coma-				
Quality Saara	free on four consecutive				
Quality Score	assessments.				
6					
	Blood was collected from each				
Risk of Bias:	patient within 48 hrs of study drug				
Unclear	initiation.				

Conclusion: A randomized, placebo-controlled trial of antipsychotics for delirium in mechanically ventilated intensive care unit patients is feasible. Treatment with antipsychotics in this limited pilot trial did not improve the number of days alive without delirium or coma, nor did it increase adverse outcomes.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Sponsored by Pfizer, Inc., No ITT, but all randomized were analyzed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = Unclear
8. Sample size ≥50 each study arm (1 point if achieved):	1		
	0		Each group around 35
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

G4-Breitbart W, Marotta R, Platt MM, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. Am J Psychiatry. 1996;153(2):231-7.

Outcomo	Adverse Effects
Outcome	Comments
earch staff monitored study patients	No significant difference
ns of delirium. Medical and nursing	-medical complications
ined. If delirium was suspected the	p<0.32
nator and study psychiatrist	-severity of complications
full assessment	p<0.61
drug treatment protocol initiated	
atients evaluated hourly with DRS,	Deaths (within 8 days of
ESRS	protocol initiation)
	n = 2 haloperidol
nt difference between treatment	n = 2 chlorpromazine
	n = 1 lorazepam
	n = 1 lorazopaln
l vs chlorpromazine vs lorazepam	Deaths within 1 week after
50 (23.1) vs 3.0 (3,.6)	completing the protocol
36.0 (18.4) vs 4.6 (4.7)	n = 3 chlorpromazine
30.0 (18.4) VS 4.0 (4.7)	n = 1 lorazepam
vo 20.62 (2.98) vo 19.22 (2.58)	II = I IOIazepaili
vs 20.62 (3.88) vs 18.33 (2.58)	Extremure midel side
vs 12.08 (6.50) vs 17.33 (4,18)	Extrapyramidal side
vs 11.85 (6.74) vs 17.00 (4.98)	effects = none
f=2,27, p<0.001	-no effect for time,
for drug NS (p<0.44)	p<0.81
	-drug by time interaction
f=1, 27, p<0.001	= trend, p<0.07
	-increase in lorazepam
<0.81 vs p<0.81	group
	Comments
	This study confirmed the
	clinical efficacy of
=1, 27, p<0.001	neuroleptic drugs in the
oved only for chlorpromazine group	amelioration of delirium
=1,27, p<0.001	symptoms in AIDS
1,27, p<0.04	patients.
	In addition, lorazepam
	alone is not effective in the
	treatment of delirium in
	AIDS patients,
	,
1,27, p<0.63	The doses of neuroleptics
	required to manage
s developed side effects	delirium in AIDS patients
confusion	may be considerably lowe
ion	than many reported in
on	clinical standards.
	onnical standards.
treatment discontinued	There may be disease
notionto rondomizad to bolonoridal	specific mechanisms that
patients randomized to haloperidol	explain why patients with
nazine	AIDS required low doses.
	ow-dose neuroleptics (haloperidol or

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Unclear	Baseline date not reported except for age and gender of 30 patients with delirium
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not clear whether outcome assessors were blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Total patients approached and number consented, but no specific data on exclusions
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	All patients analyzed, but ITT protocol not performed Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low risk of bias:

   o
   Unclear risk of bias:
   High or unclear risk of bias on 1 or more of 6 domains

   ٠

  - High risk of bias: High risk of bias on 2 or more of 6 domains

G3-G5-Lundstrom M, Edlund A, Karlsson S, et al. A multifactorial intervention program reduces the duration of delirium, length of hospitalization, and mortality in delirious patients. J Am Geriatr Soc. 2005;53(4):622-8.

O fair all a	Denviation	Internetien Orecord		Results	0
Study	Population	Intervention Groups	Measure	Outcome	Comments Conclusion
Characteristics			Dellature en	TI (11 11 1 000 1 1	
Lundstrom M 2005	N = 400	n = 200 Intervention group	Delirium assessment:	Three of the authors rate OBS scale and	Too few patients had
Sweden			DSM-IV	MMSE on days 1,3, and 7, then determined	dementia in the present study
	Inclusion	Men /women% 39.0/61.0		delirium according to DSM-IV criteria (90%	to allow analyses of patients
Setting	Age ≥70	Mean age 79.4 (5.6)		inter-rater agreement) (authors blinded to	with dementia separately, but
Department of	Informed consent			allocation)	no patient with dementia
Seneral Internal		1. A 2-day course for staff on			remained delirious on Day 7 in
Medicine, University	Exclusion	geriatric medicine focusing on	Baseline characteristics	Significant difference between groups	the intervention ward,
Hospital	N = not described	assessment, prevention, and		Intervention vs control	compared with four patients
	Age <70	treatment of delirium	Age	79,4 (5.6) vs 80,7 (6.2), p=.02	still delirious on Day 7 in the
Study Design	Declined participation		Male% vs Female %	39.0%/ 61.0% vs 49.5%/50.5%, p=.04	control ward, which might
Prospective	Declined participation	2. Education concerning caregiver-	Diabetes mellitus	42.5% vs 23.5% p<0.001	indicate that delirium in
	Other coccernent (all	patient interaction focusing on			
controlled clinical trial	Other assessment (all		Stroke %	170% vs 25.0%, p=05	patients with dementia can be
	patients):	patients with dementia and	Myocardial infarction	10% vs 4.5%, p=.03	successfully treated.
Selection method	RA assessed on Days 1,	delirium			
Consecutive	3, and 7 after admission		Logistic Regression to	Delirious Patients in the Two Wards	
dmission to 2 wards	Organic Brain Syndrome	3. Reorganization from a task-	Control for Baseline	(N=125; n = 63 vs n = 62))	Limitations
ntervention ward;	(OBS) Scale,	allocation care system to a patient-	Differences		-randomization/allocation
ontrol ward)	MMSE	allocation system with	Ward	OR=3.12 (1.43–6.81)	dependent on bed availability
Random allocation	Katz ADL index	individualized care	Stroke on admission	OR=1.44 ( 0.62–3.35)	-RA assessors not blinded
rom ED based on	Vision testing		Sex	OR=1.35 (0.59–3.05)	-assessments not done daily
	3	4. Quidance for pursing staff anes			5
available bed;	(admission)	4. Guidance for nursing staff once	Age	OR=1.01 (0.95–1.08)	-discharged patients
eadmissions within 3	Hearing testing	a month	Diabetes mellitus	OR=0.53 (0.22–1.27)	regarded as not delirious on
nonths of discharge	(admission)				Day 7 (1 patient assessed as
admitted to the same		No blinding	Primary outcomes	Day 1 vs Day 3	delirious within 24 h of
vard as previous			Delirium incidence	123/400 (30.8%) vs 82/400 (20.5%),p <.001	discharge)
reatment				Intervention vs control	
			Delirium prevalence (24h)	31.5% vs 31.0%; p=.91	
Study Length/Start-			Delirium incidence (Day3)	58.7% vs 72.6%; p=.10	
Stop Dates			Delirium incidence (Day7)	30.2% vs 59.7%; p=.001	Conclusion
Not described			Definition incluence (Dayr)	30.2 /0 V3 33.1 /0, p=.001	Conclusion
NOT DESCRIDED			Secondamy systematics	Intervention we control	This study shows that a
<b>-</b>			Secondary outcomes	Intervention vs control	This study shows that a
Purpose			Length of stay( days)	9.4 (8.2) vs 13.4 (2.3); p<.001	multifactorial intervention
Fo investigate			Return to home/apt	86.6% vs 82.4%; p=.29	program reduces the duration
whether an education					of delirium, length of hospital
program and a			Delirious patients		stay, and mortality in delirious
eorganization of			Return to home/apt	78.3% vs 60%; p=.05	patients.
nursing and medical			Mortality	2 (3.2%) vs9 (14.5%); p=.03	
are improved the			,		
outcome for older		n = 200 Control group	Delirium assessment:		1
elirious patients.					
		Men/women % 49.5/50.5		See above	
unding source(s):			Baseline		
oint Committee of		Mean age 80.7 (6.2)	characteristics/measures		
			characteristics/measures		
neNorthern Health		Usual hospital care organized in a			
Region of Sweden		task-allocation care system;			
Visare Norr), et al		-the same caregiver handled	Primary outcomes		
		particular tasks for all patients,			
Quality Score		-no clinical caregiver had full	Secondary outcomes		
-		responsibility for an individual			
		patient during his or her entire			
Risk of Bias:		hospitalization.			
High		Staff aware that a series of			
		Staff aware that a screening of			
		delirium prevalence was being			
	1	performed		1	85

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Randomization based on bed availability; significant baseline differences between groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Allocation concealed only for authors who determined delirium dx
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	No blinding except authors who determined delirium dx
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	No information on number of patients excluded
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Numerous baseline imbalances, but analyzed to determine OR related to delirious patients Unknown confounders possible because delirium assessment not done daily
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-Zaubler TS, Murphy K, Rizzuto L, et al. Quality improvement and cost savings with multicomponent delirium interventions: replication of the Hospital Elder Life Program in a community hospital. Psychosomatics. 2013;54(3):219-26.

C to a to a	Denviletter	Internetica Oracia		Results	0
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Zaubler TS 2013 USA Setting General medical floor at a community hospital Study Design Quality improvement study (Pre-Post design) Selection method Patients admitted to general medical floor Study Length/Start- Stop Dates 11/2010 – 2/2011 (pre)	N = 595 enrolled Inclusion -All patients age ≥ 70 -with or without delirium on admission NOTE: usual HELP requirement for 1 delirium risk factor other than age not implemented in this study Exclusion N = not discussed Not likely to benefit from the interventions	n = 380 Intervention (7/2011-3/2012) Men and women (61%) Mean age 83.2 (6.6) Protocol -Patients received interventions from the Elder Life Specialists or volunteers, on weekdays, 5 days per week, adapted from the original HELP model -Exercise/mobility protocol was omitted because of staffing limitations Adapted HELP program interventions and activities	Delirium assessment: CAM Baseline characteristics Primary outcomes Delirium episodes Patient days w/ delirium All patients LOS(d) mean LOS For non-delirious patients (n=506)	After screening assessment, CAM administered twice daily on weekdays (medical record reviewed for delirium on weekends and holidays) Elder Life Specialist usually administered CAM (description vague) No significant difference between groups <b>Pre-Intervention vs. Intervention</b> 20% vs. 12% p=0.019 129(8%) vs. 123(6%) p=0.005 7.4(6.4) vs. 5.2(4.2) p<0.001 7.2(6.2) vs. 5.0(4.1) p<0.001	Since it is exceedingly difficult in a community hospital setting to maintain HELP interventions more than 5 days per week, it was often impossible to discriminate between prevalent (pre-admission) and incident (arising after admission) delirium The HELP interventions, therefore, were not limited to those without delirium at the time of the first assessment as was the case in other studies. Overall LOS among all patients enrolled in the intervention group decreased by 2 days.
7/2011 – 3/2012 (post) <b>Purpose</b> To implement an adapted HELP program in a community hospital and to prospectively assess its effectiveness and cost impact in this setting. <b>Funding source(s):</b> Grants from Head Charitable Foundation and the Marion E. C. Walls Trust	-Non-verbal - terminal illness -refused to participate All patients Assessed with CAM Brief cognitive screen (not identified) Digit Span Test Training Volunteer recruitment (beginning 11/2010) Trained in HELP core interventions Supervised by Elder	-Daily visits -Therapeutic activities -Feeding assistance -Hydration assistance -Vision/hearing protocol -Sleep assistance <b>n = 215 Pre-intervention</b> (11/2010-2/2011) Men and women (63%) Mean age 82.2(7.3) <b>Protocol</b> Usual care	Financial Outcomes Savings (variable costs) Revenues (potential increase) Total Delirium assessment: Baseline characteristics Primary outcomes	Study (9 months) / Annualized \$81,000 / \$108,000 \$760,000 / \$1,014,000 \$841, 000 / \$ 1,112,000 See above See above See above	Interestingly, the LOS for patients without delirium had a highly significant 1-day reduction in LOS. This suggests that HELP benefits non-delirious patients, possibly by minimizing physical or cognitive decline during hospitalization and/or improved coordination of care and dis- charge planning with the inclusion of the Elder Life Specialists in clinical rounds. Another compelling outcome was
Quality Score 3 Risk of Bias: High	Life Specialists <b>Cost savings</b> Comparisons between delirium and no delirium patients Variable costs compared for patients with dx of pneumonia Potential increased revenue calculated based on LOS				the annual cost savings of \$1,122,000. This more than offsets the cost of the salary of the two Elder Life Specialists and minimal sup plies that were purchased (\$96,763). Limitations -assessments and interventions only on weekdays -difficult to discriminate betweet prevalent and incident delirium -no concurrent control group

**Conclusion**: HELP can be successfully adapted for implementation in a community hospital setting to decrease delirium episodes, total patient-days with delirium and LOS, and generate substantial cost savings.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Pre/post study design (no matching)
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Pre/post study design
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Pre/post study design; outcome assessors not blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	No detail on excluded patients
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Historical controls Pre/post design Intervention implemented only on weekdays
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):	1		BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-G5-Rubin FH, Williams JT, Lescisin DA, et al. Replicating the Hospital Elder Life Program in a community hospital and demonstrating effectiveness using quality improvement methodology. J Am Geriatr Soc. 2006;54(6):969-74

Otherstein	Demulation	Internetic - Original		Results	0
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
RubinFH 2011	N = 1929	n = 704 HELP Intervention	Delirium assessment:	A nurse practitioner evaluated patients	
JSA	n = 1225 baseline (pre-	Time period: 7/2002 – 12/2002	Specific assessment tools	for the presence of delirium and for the	Factors contributing to success
	intervention)	- F	not described	presence of modifiable predisposing or	Shadyside included
Setting	n = 704 post	Men and women (63.5%)		precipitating factors. She interacted with	-a long tradition of QI
Community teaching	intervention	Mean age 80.9 (6.7)		staff nurses and treating physiciabns.	improvements for elderly
ospital				stan haroes and treating physiolashs.	inpatients;
loopital	Inclusion	Phase in data collected 1/2002			-inclusion of all stakeholders ir
Study Design	Aged ≥ 70	through 6/2002	Baseline characteristics	Significant difference between groups	the project, especially nursing a
Pre-test/post-test quality	Admitted to Hospital	11100g110/2002	Dasenne characteristics	Baseline vs HELP	ancillary personnel, so that
	Elder Life	HELP implementation 7/2002-	Cerebrovascular disease	7.4% vs 3,7%, p .001	concerns of competition or "tur
mprovement study		12/2002	Gastrointestinal disease		•
	Fuelusian	12/2002		5.1% vs 12.4%, p <.001	were resolved at the outset;
Selection method	Exclusion		Ischemic heart disease	2.7% vs 4.5%, p .04	-an accompanying educationa
Patients admitted to a	N = not discussed	Protocol	Renal failure	0.4% vs 1.4%, p .03	campaign to generate support;
nursing unit	-Diagnosis of	Hospital Elder Life Program			-an identified senior physician
	schizophrenia	Daily interventions targeted	Primary outcomes	Baseline vs. Intervention	champion;
Study Length/Start-	-Baseline use of major	patients were not delirious and	Delirium rates	40.8% vs. 26.4% p < .002	-use of data that hospital
Stop Dates	tranquilizers	who were at intermediate risk for			leadership found credible;
2001 - 2002		developing delirium			<ul> <li>agreement with management</li> </ul>
			Financial outcomes		the outset on what outcomes
Purpose	HELP Implementation	Risk factors present:	Est 101 cases prevented	\$220,281 cost savings	would be important;
o evaluate a replication	personnel	<ul> <li>cognitive impairment</li> </ul>	14.4% reduction in delirium		<ul> <li>beginning with only one unit;</li> </ul>
of the Hospital Elder Life	-Elder life specialist	-sleep deprivation	rate	364 bed-days saved	-institution-wide celebration of
Program (HELP), a	(1.0 FTE)	-immobility	Net cost savings (cost		results.
quality-improvement	-clinical geriatrician	-visual or hearing impairment	savings -cost of		
nodel, in a community	(0.1 FTE)	-dehydration	HELP)	\$562,611 in 6 mos on one 40-bed	
nospital without a	-geriatric nurse		,	nursing unit	
esearch infrastructure,	practitioner (0.5 FTE)	Deviations from the original	Nursing satisfaction		
using administrative data	, ,	HELP model	outcomes		
C		-exercise and fluid repletion	Nurses and nurses' aides		
Funding source(s):		protocols omitted due to	Agreed	"My job is more satisfying due to HELP"	
Shadyside Hospital		insufficient staffing	Highly agreed	"It would be helpful to make HELP a	
		-sleep protocol modified		permanent program on my unit"	
Foundation funded the		-the Role of the nurse		P P 3	
Shadyside replication.		practitioner was modified to	Patient satisfaction with		
he HELP dissemination		eliminate redundancies with	HELP	2.8/3 rating for overall satisfaction	
effort was funded in part		existing services			
by grants from the		chicang connect			
National Library of					
Medicine, the Commonwealth Fund		n = 1,225 Baseline (control)	Delirium assessment:	See above	1
		Time period: 1/2001 – 12/2001	Deminan assessment.		
he Fan Fox and Leslie			Baseline characteristics		
R. Samuels Foundation),		Men and women (63.8%)		See above	
and the Retirement		Mean age 80.6 (6.2)	Primary outcomes		
Research Foundation.		wear age 00.0 (0.2)	Finiary outcomes	See above	
		Baseline data measured	Secondary outcomes		
Quality Score:			Secondary outcomes	See above	
3		throughout 2001		See above	
		Drotocol			
Risk of Bias: High		Protocol Standard care			

Conclusion: Conclusion: HELP can be successfully replicated in a community hospital, yielding clinical and financial benefits

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Individuals not randomized or individual matched. Differences between groups
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Allocation not concealed due to different time periods
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Outcome assessors not blinded
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Pre/post design Cohorts were assessed at different time periods and thus there may be other confounding variables
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	0		Delirium assessment tool not described
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on <u>the criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

# G3-G5-Inouye SK. Prevention of delirium in hospitalized older patients: risk factors and targeted intervention strategies. Ann Med. 2000a;32(4):257-63.

Study Characteristics	Population	Studies	Measure	Outcome	Other information
Inouye 2000a USA Setting General medicine service at a university hospital	Delirium Prevention Trial N = 852 enrolled n=426 matched pairs of intervention-control patients	To identify predisposing factors for developing of delirium during hospitalization n = 107 patients first cohort n = 174 second cohort (validated first cohort findings)	<ul> <li>&gt;30 potential risk factor variables studied</li> <li>Predisposing risk factors</li> <li>Vision impairments (acuity &lt;20/70)</li> <li>Severe illness (APACHE II &gt;16)</li> <li>Cognitive impairment (MMSE &lt;24)</li> <li>Debudration (PLIN/CPL artio &gt; 19/</li> </ul>	RR 3.5 (1.2 – 10.7) RR 3.5 (1.5 – 8.2) RR 2.8 (1.2 – 6.7) RR 2.0 (0.9 – 4.6)	Patients placed in low (no factors present), intermediate (one or tw factors present), or high (three or four factors present) risk groups showed a statistically significant trend towards increasing risk of delivium with increasing rumbers
Study Design -prospective studies to examine predisposing and precipitating factors for delirium, -controlled clinical trial intervention using	<b>Inclusion</b> Age ≥ 70 -no evidence of delirium at admission -intermediate to high risk for delirium at baseline	Inclusion Age ≥ 70 -admitted to general medicine service at a university hospital	Dehydration (BUN/CR ratio ≥ 18(		delirium with increasing numbers of predisposing factors. RR for delirium increased from 1.0 in lov risk group to 9.2 in high-risk group. -predictive model and risk stratification system validated in the second cohort of patients
prospective individual matching Selection method Delirium Prevention Trial: consecutive patients admitted to general medicine service at	Exclusion Not discussed ****** Delirium Prevention Trial Prospective matching	Examine precipitating factors for delirium during hospitalization. Two prospective cohorts of consecutive patients aged 70 years and older admitted to general medical service n = 196 first cohort	Develop and validate a predictive model for delirium based on noxious insults or factors occurring during hospitalization >25 candidate risk factor variables studied		Study demonstrated distinct risk gradients, with patients placed in low, intermediate, or high-risk groups showing a statistically significant trend towards increasing risk of delirium with increasing numbers of precipitating factors.
Study Length/Start-Stop Dates Not discussed	strategy to assure comparability of patients between intervention and control groups	n = 312 second cohort Inclusion Age $\ge 70$ -admitted to general medicine	Precipitating factors Use of physical restraints Malnutrition More than 3 medications added Use of bladder catheter	RR 4.4 (2.5 – 7.9) RR 4.0 (2.2 – 7.4) RR 2.9 (1.6 – 5.4) RR 2.4 (1.2 – 4.7)	RR for delirium increased from 1.0 in the low-risk group to 22.7 i the high-risk group. -validated in the second cohort o patients which produced similar.
Purpose To describe the multifactorial etiology of delirium; to elucidate the	Protocols for targeted risk factors Cognitive impairment -reality orientation	service at a university hospital Intervention group = 426 Delirium Prevention Trial Intervention (Hospital Elder	Any iatrogenic event Incidence of delirium	RR 1.9 (1.1 – 3.2) Intervention vs. control 9.9% vs. 15% OR .6 (0.39- .92)	statistically significant risk gradients. No adverse effects were associated with any intervention protocols
predisposing and precipitating factors for delirium derived from earlier work; and to present an overview of the Delirium Prevention Trial, which was targeted to address delirium risk	-therapeutic activities Sleep deprivation -noise reduction -uninterrupted slep Immobility -early mobilization -minimize immobilizing equipment	Life Protocol) Intervention (see Protocols for targeted risk factors) Standardized protocols targeted towards six delirium risk factors. Delirium assessment:	Days of delirium Total no. episodes of delirium Rate of adherence to all intervention protocols Adherence rate for individual intervention protocols	105 vs. 161 p = 0.02 62. vs., 90 p = 0.03 87% 71% - 96%	Through the identification of risk factors and targeting intervention strategies towards them, we have been successful in preventing delirium in hospitalized older patients, reducing the risk of delirium by 40%.
factors. Funding source(s): Grants from NIA and Patrick and Catherine Weldon Donaghue Medical Research Foundation	Visual impairment -vision aids -adaptive equipment Hearing impairment -amplifying devices -hearing aids -wax disimpaction Dehydration	Assessment tool: CAM All patients assessed daily by RAs who had no role in the intervention unaware of intervention or study group assignment	reduction in the total number of risk factors per patient compared with the usual care group at reassessment Improvement in the orientation score of patients with cognitive impairment	p = 0.001 40% vs 26% improved;	Results suggest that primary prevention of delirium, (preventin delirium before it occurs), may be the most effective treatment strategy for delirium, a finding which holds substantial clinical
Quality Score: 7 Risk of Bias:	-early recognition -volume repletion	<b>Control Group = 426</b> Protocol = Usual care with daily delirium assessment	at admission Reduction in the rate of use of sleep medications in all patients	p = 0.04 46% vs 35%; p = 0.001	and health policy implications for delirium management in specific and for the geriatric population more generally.
Unclear			owards them, we have been successful i	NOTE: Specific recommendations for delirium prevention detailed in PDF	

of delirium by 40%.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not discussed
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-G5-Lundstrom M, Olofsson B, Stenvall M, et al. Postoperative delirium in old patients with femoral neck fracture: a randomized intervention study. Aging Clin Exp Res. 2007;19(3):178-86.

				Results	<b>•</b> .
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Lundstrom M 2007	N = 353 patients	n = 102 Intervention	Delirium assessment:	Delirium assessments by study nurses	Multivariate linear regression
Sweden	assessed for eligibility	n = 6 patients died during	MMSE	daily postop days 1-7; blinded specialist	to control for baseline
	n = 154 excluded	hospitalization	Organic Brain Syndrome Scale	in geriatric medicine analyzed all	differences
Setting	N = 199 randomized	n = 92 assessed at 4 months	(OBS)	assessments and documentation once	Dependent variable = number
University hospital	and analyzed	n = 86 assessed at 12 months	DSM – IV	during hospitalization	of days with postop delirium
					Independent variables (p)
Study Design	Inclusion	Men and women (72.5%)			-delirium post op (<0.001)
RCT	-Age ≥ 70	Mean age 82.3 (6.6)	Baseline characteristics	No significant differences, except:	-control group (0.001)
	-Consecutively admitted			Intervention vs. Control	-male sex (0.004)
Randomization method	to Orthopedic	Protocol	Depression	32.4% vs. 47.4%, p 0.031	-depression (NS)
Sealed envelope.	Department	-Patients randomized to the	Antidepressants	28.4% vs.46.4%, p 0.009	-dementia (NS)
Stratified according to	-Femoral neck fracture	intervention group were			-age (NS)
dislocation of fracture.		admitted to a 24-bed geriatric	Primary outcomes	Intervention vs. Control	
	Exclusion	unit specializing in geriatric	Days postoperative delirium	5.0 (7.1) vs. 10.2(13.3) p =0.009	Despite some baseline
Study Length/Start-	N = 154	orthopedic patients.	Patients delirious postop	54.9% vs. 75.3% p=0.003	differences between the
Stop Dates	n = 95 did not meet	-The staff applied	Significant difference between		intervention and control groups,
5/2000 - 12/2002	inclusion criteria	comprehensive geriatric	groups for each day (1-7)	p =0.001	there was still a strong
	n= 11 Refused to	assessment, management	Delirious after the seventh		association between number of
Purpose	participate	and rehabilitation	postoperative day	18% vs. 52% p< 0.001	days with postoperative delirium
To determine whether a	n=27 missing due to		Delirious at discharge	0 vs. 20 patients p < 0.001	and being treated in the control
postoperative multi-	failed inclusion routines	Main content of intervention	-		group.
factorial intervention	n = 21 suffered fracture	protocol	Secondary outcomes	Intervention vs. Control	
program, including	in hospital	-Staff education	Urinary infections	39.3% vs. 60.3% p =0.018	The effect of the intervention
comprehensive geriatric	-severe rheumatoid	-Teamwork	Sleeping problems	28.6% vs. 50.7% p = 0.011	program seemed to reduce the
assessment,	arthritis	-Individual care planning	Falls	17.9% vs. 34.3% p = 0.034	incidence of delirium on the first
management and	-severe hip	-Delirium prevention,	Decubitus ulcers	10.7% vs. 23.6% p=0.059	postoperative day.
rehabilitation, can	osteoarthritis	detection, treatment	Assessments of underlying		
reduce delirium and	-severe renal failure	-Prevention/treatment of	causes of delirium		This may be explained by the
improve outcome in	-pathological fracture	complications	documented in		fact that, when the patients
patients with femoral	-patients who were	-infection	medical records	2.28(1.25) vs. 0.90(0.90) p<.001	arrived at the intervention ward,
neck fractures.	bedridden before	-anemia	Length of Stay (LOS) (days)	28(17.9) vs. 38(40.6) p= 0.028	they were immediately and
	fracture due to the	-embolism	LOS for patients with postop		systematically assessed to
Funding source(s):	operation methods that	-Bowel/bladder function	delirium	31.4(19.3) vs. 43.6 (42.7) p= 0.032	detect, treat and prevent any
Vardal Foundation, Joint	were planned to be		LOS for delirium patients with		complications that would cause
Committee of the	used in the study		dementia	3.2 (4.1) vs 12.8 (17.6), p = 0.003	delirium.
Northern Health Region			Dementia patients with postop		
of Sweden , JC Kempe			delirium at discharge	0 vs 15, p <0.001	Patients with dementia seemed
Memorial Foundation,	Other assessments				to have benefited from the
Foundation of the	Geriatric Depression	n = 97 control	Delirium assessment:	See above	intervention program.
Medical Faculty,	Scale (GDS)		Baseline characteristics	See above	
University of Umeå,	Prefracture Personal	Men and women (76.28%)	Primary outcomes	See above	All parts of the intervention
County Council of	ADLs (P-ADL)	Mean age 82 (5.6)	Secondary outcomes	See above	program, which are probably
Västerbotten and					equally important should be
Swedish Research		Protocol	Delirious control patients		systematically adapted with
Council, Grant		Usual postoperative care in	received		focus of detection, prevention
		the orthopedic department	More sedatives	41.7% <i>vs</i> 15.4%, p=0.008	and treatment of delirium
Quality Score:			More opioid drugs on demand	61.7% <i>v</i> s 30.8%, <i>p</i> =0.004	
6		Patients needing further in-			Limitation
		hospital rehabilitation (n = 40)			-psychiatric symptoms and
Risk of Bias:		admitted to a geriatric ward			cognitive testing only 1 time
High		but not the intervention ward			during hospitalization

**Conclusion**: This study shows that postoperative delirium can be successfully treated by a team applying comprehensive geriatric assessment, management and rehabilitation. The intervention program resulted in fewer days with delirium, fewer other complications, and shorter hospital stays. Implementing this intervention program will probably have a great humanitarian and economic impact, and is probably applicable to surgery on old people in general. Therefore, the organization of surgical wards should be reconsidered and adapted to the needs of the oldest and frailest patients.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Significant differences in baseline characteristics
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	No blinding during outcome assessment (record reviews)
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G3-G5-Milisen K, Foreman MD, Abraham IL, et al. A nurse-led interdisciplinary intervention program for delirium in elderly hip-fracture patients. J Am Geriatr Soc. 2001;49(5):523-32.

,	, ,			erly hip-fracture patients. J Am Geriatr Soc. 2007 Results	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Milisen K 2001	N = 120 patients	n = 60 intervention cohort	Delirium assessment:	Trained research nurses obtained	There was neither a statistical
Belgium	analyzed	(9/1997 – 3/1998)	CAM	information about cognitive functioning	nor clinical effect for the
	n = 60 pre-intervention		MMSE	(CAM and MMSE) on the first, third, fifth,	intervention relative to functional
Setting	n = 60 post-intervention	Men and women (81.7%)		eighth, and twelfth postoperative days.	status.
Urban academic		Median age 82 (13)			
medical center	Inclusion		Baseline characteristics	Significant differences :	There was no significant
	-Patients admitted to the	Overview		Intervention vs. Control	difference in functional status
Study Design	ER w/ traumatic fracture of	<ul> <li>A system of enhanced</li> </ul>	Cardiac comorbidity	13.3% vs. 30% p=.045	between the intervention and
Prospective	proximal femur (intra-and	quality of nursing care for	Vascular comorbidity	5% vs. 25% p=.004	control cohorts or for either the
longitudinal (pre/post	extracapsular)	older hip- fracture patients	Abdominal comorbidity	5% vs. 20% p=.025	delirious or nondelirious patients.
design)	-Hospitalized in one of two	was developed,			
	traumatological nursing	implemented, and tested.	Primary outcomes	Intervention vs. Control	However delirious patients in
Selection method	units w/in 24 h of surgery	-Nurses identified high-risk	Incidence of delirium, n%	12 (20.0%) vs 14 (23.3%) (p = 0.82 – NS)	both cohorts were more
Patients admitted to	-Spoke Dutch and verbally	patients and provided			dependent after discharge and 3
ER with traumatic	testable	prompt anti-delirium	Duration of delirium (days)	1 (1) vs. 4 (5.5), p=.03	months after discharge.
fracture of proximal		interventions to reduce and			
femur	Exclusion	treat delirium.	Severity of delirium		Neither cohort of the delirious
	-Multiple trauma	-Access to readily available	Mean total CAM scores	Delirium vs no delirium	patients regained their pre-
Study Length/Start-	concussion of the brain	consultants and were able to	Intervention group range	3.82 (2.8) to 1.91 (2.3) vs 0.98 (1.6) to 0.87	fracture functional status.
Stop Dates	-Pathological fractures,	administer regularly		(1.7)	
9/1996 - 3/1997	surgery occurring more	scheduled pain medications.	Control group range	6.92 (2.8) to 5.0 (3,.1) vs 1.35 (2,.3) to 0.76	Delirious patients in both cohorts
9/1997 - 3/1998	than 72 hours after		5 1 5	(1.4)	also had a slower functional
	admission, aphasia, -	Protocol components	Linear mixed model analysis	$\dot{p} = 0.0152$ , intervention vs control	rehabilitation over time.
Purpose	blindness	1. Education of nursing staff		No significant difference in change over time	
To develop and test	-Deafness	2. Systematic cognitive		5	There was no significant
the effect of a nurse-	-Fewer than 9 years of	screening		Significant difference in decrease in CAM	difference in length of stay
led interdisciplinary	formal education	3. Consultative services by		scores over time (less severity) in both	between intervention and control
intervention program		-delirium resource nurse		cohorts ( $p = 0.0013$ )	groups or between delirious and
for delirium on the		-geriatric nurse specialist			nondelirious patients
incidence and course		-psycho-geriatrician		On average the CAM scores decreased by	
(severity and		4. Use of a scheduled pain		0.082 units a day	Limitations
duration) of delirium,		protocol		, , , , , , , , , , , , , , , , , , ,	-pre/post study design
cognitive functioning,			Cognitive function	Intervention vs control	-less control of confounding
functional			Sub-dimension memory	p = 0.0357 (see figure 4)	variables
rehabilitation,				Delirium vs no delirium	-use of medical records to
mortality, and length			Memory improvement over	p = 0.0001 (both cohorts)	obtain historical data
of stay in older hip-			time		
fracture patients.			Intervention effect on		
			memory	p = 0.0087	This study demonstrated the
Funding source(s):			Overall cognitive functioning	both cohorts <b>Delirium vs no delirium</b>	beneficial effects of an
The Ministry of Public			improved	p = 0.0001 and p 0.0026	intervention program focusing on
Health and		n = 60 pre-intervention	Delirium assessment:	See above	early recognition and treatment of
Environment of the		cohort (control)			delirium in older hip-fracture
Belgian Government		(9/1996-3/1997)	Primary outcomes	See above	patients, with the delirious
Bolgian Covonnion					patients in the intervention cohort
Quality Score		Men and women (80%)			showing less severe delirium,
4		Median age 80 (12)			shorter duration of delirium, and
					fewer memory problems.
Risk of Bias:		Protocol			
High		Usual care			

**Conclusion**: This study demonstrated the beneficial effects of an intervention program focusing on early recognition and treatment of delirium in older hip fracture patients and confirms the reversibility of the syndrome in view of the deliriums duration and severity.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Significant differences in baseline characteristics
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Pre/post design - no blinding
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Pre/post design – no blinding
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Pre/post study with historical controls Baseline imbalances Possibility of confounding variables
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

# G3-G5-Rubin FH, Neal K, Fenlon K, et al. Sustainability and scalability of the hospital elder life program at a community hospital. J Am Geriatr Soc. 2011;59(2):359-65

<b>e</b>				Results	
Study Characteristics	Population	Study Process	Measure	Outcome	Comments
Rubin 2011	Patients served (year)	Intervention	Delirium assessment:	2002-2004 proxy assessment process	The multiplicative expansion of
USA	N = 940 (2002)	HELP initiated in 2002	CAM	validated by geriatricians and nurse	the program during the 7 years
	N = 4,044 (2005)	Disseminated and expanded		practitioners. Beginning in 2004 direct	reported attests to the scalability
Setting	N = 27,196 (2008)	2003 – 2008		bedside assessment using CAM	and generalizability of the HELP
Community teaching		-adoption of healthcare		-	interventions.
hospital	HELP units	innovations	Baseline data	2001 (before HELP)	
•	2002 = 1 unit; 40 beds	-strong clinical leadership	Delirium rate	41%	This program implementation
Study Design	2008 = 6 units. 184 beds	-support of senior		Other baseline date not reported in this	demonstrated important positive
Quality improvement	2000 0 0	management		paper.	outcomes in terms of
project	HELP staffing (FTEs)	-credible supportive data		papon	-improving clinical care
project	2002 = 1.8  FTEs	-infrastructure supportive of	Primary outcomes	2002 / 2005 / 2008	(reduction of delirium),
Selection method	2002 = 1.6 FTEs		Delirium rate %	2002/2003/2008	
		innovation		000/ 1400/ 1400/	-enhancing staff and patient
Patients aged 70 and	2008 = 7.5 FTEs	-organizational culture	(incident + prevalent)	26% / 16% / 18%	satisfaction with care,
older on this unit who		change			-shortening hospital LOS
met the HELP criteria	HELP volunteers	-effective interdepartmental	Reduction in delirium,		- reducing costs of care,
were enrolled	2002 = 24	and interdisciplinary	percentage points	-15% / -25% / -23%	-fulfilling important clinical
	2005 = 52	collaboration			effectiveness and quality
Study Length/Start-	2008 = 107	-responsive to immediate	Incident delirium 2004-2008	≤3% from 2004 to 2008	improvement goals
Stop Dates		pressures and threats			-enhancing efficiency on a large
2001 - 2008	HELP volunteer		Patient satisfaction (range 1-3)	2.8 / 2.8 / 2.9	scale within the hospital.
	interventions (estimate)				
Purpose	2002 = 5381	Protocol	Nurse satisfaction (range 1-3)	4.8 / 4.5 / NA	The low rate of incident delirium
To describe the	2005 = 24,000	Hospital Elder Life	Naise satisfaction (range 1.0)	4.074.07107	(3%) among enrolled patients
evolution of the HELP	2008 = 41, 880	Program (from 2002	Reduction from baseline in		might represent a benchmark for
	2008 – 41, 880				
program at Shadyside	la charten	description)	LOS	0.0(4.0) (NA (7.0.(0.0)	delirium reduction programs.
over the 7- year	Inclusion	Daily interventions targeted	Patients with delirium (days)	8.8(1.0) / NA / 7.0 (2.8)	
period from 2002 to	Age ≥ 70	patients were not delirious			The low rates of observed
2008, including the	Met HELP Criteria	and who were at	Patients without delirium	6.0 (0.1) / NA / 5.3 (0.8)	delirium (≤3%) from 2004 to
adaptations, patient		intermediate risk for			2008, which are lower than
outcomes, cost	Exclusion	developing delirium	Cost saving, per year, \$	1.23 million / NA / 7.37 million	observed rates in previous
savings, challenges,	Dx schizophrenia				studies of HELP, may have been
and successes	Using major tranquilizers/	Risk factors present:	Challenges	Solutions/outcomes	a reflection of the inclusion of
	antipsychotics	-cognitive impairment	Staff turnover	Define roles, recruitment	lower-risk patients in that sample
Funding source(s):	Physical restraint during	-sleep deprivation	Personnel conflicts	Team building efforts	and the once-a-day clinical
Funded in part by	hospitalization	-immobility	Volunteer turnover	Enhance recruitment; academic credit for	delirium assessments (as
Grants from the NIA,		-visual or hearing		volunteers	opposed to daily research
from the Retirement		impairment	Broad geographical coverage	Develop satellite offices; stock offices with	assessments augmented by
Research Foundation,		-dehydration	broad geographical coverage	computers and supplies;	nursing interviews and medical
		-denydration	Depenverts reduction and	Develop more efficient software and	
from the Alzheimer's		Deviations from the original	Paperwork reduction and		record reviews in previous
Association, and the		Deviations from the original	tracking	database system for volunteer	studies).
Aging Brain Center,		HELP model		assignments and data collection	
Institute for Aging		-exercise and fluid repletion	_		The financial return of the
Research, Hebrew		protocols omitted due to	Success	Solutions and outcomes	program, estimated at more than
Senior Life		insufficient staffing	Met defined success metrics	Hospital-wide dissemination to 6 units	\$7.3 million per year during 2008
		-sleep protocol modified	Prevention of delirium and	Grand prize for hospital's Quality	comprises cost savings from
Quality Score:		-the Role of the nurse	shorter LOS	Improvement in 2003 and 2007	delirium prevention and revenue
3		practitioner was modified to	Volunteer recognition	Volunteers receive widespread	generated from freeing up
-		eliminate redundancies with		commendation, at hospital and local	hospital beds (shorter LOS of
Risk of Bias:		existing services		newspaper	HELP patients with and without
NA – descriptive					delirium).
•					
report					

**Conclusion**: The present study now makes the dissemination and financial case for HELP, which should clearly be a priority area for hospitals. In addition to preventing delirium, the program is effective for other important quality indicators, including falls, pressure ulcers, and LOS. The rising numbers of elderly inpatients compel all hospitals to carefully address their approaches to the population and to seriously consider HELP. This study can serve as a useful model for the successful implementation and dissemination of HELP.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouve et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	QI study
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ol> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ol>	0	Unclear	QI study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	QI study
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Historical controls
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

# G5-Cole MG, Primeau FJ, Bailey RF, et al. Systematic intervention for elderly inpatients with delirium: a randomized trial. CMAJ. 1994;151(7):965-70.

Study	Population	Intervention Groups	Measure	Results Outcome	Comments
Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Cole MG 1994	N = 174 SPMSQ ≥5	n = 42 treatment group	Delirium assessment:	Initial CAM assessment by study	Disposition of 88 patient
Canada	N = 88 dx with delirium	n = 3 discharged or died before RA first	CAM	nurse for delirium dx per DSM III;	at 8 weeks
Janada		assessment	DSM III	enrollment and randomization if	- 44 discharged from
	la aluai an				5
Setting	Inclusion	n = 39 analyzed	SPMSQ	positive for delirium. After random	hospital
Jniversity-affiliated	Age ≥75		CGBRS	allocation, a blinded RA completed	<ul> <li>13 remained hospitaliz</li> </ul>
Hospital	Admitted to medical	Men and women (71.4%)		the 1 <sup>st</sup> assessment using SPMSQ	- 31 died (35%)
	department	Mean age 86.8 (5.9)		and CGBRS; RA reassessed for	
Study Design	English or French			delirium on weeks 1, 2, 4, and 8	No significant difference
RCT	language	Consultation by a geriatrician or geriatric			between groups
	Score ≥5 on SPMSQ	psychiatrist	Baseline characteristics	Significant differences	-use of restraints
Randomization		-within 24 h after referral		Treatment vs control	-LOS
	Exclusion		Conder (more women)	71.4% vs 58.7%	
nethod		-chart review	Gender (more women)	71.4% VS 50.7%	-discharge rate
Randomly allocated to	N = 488	-interview with patient or family			-discharge to a setting
reatment or control	n = 47 ICU admission	-interview with clinical staff	Outcomes	Treatment group	providing higher level of
group by blinded RA	n = 84 cardiac	-determine previous med and psych hx	Delirium alone	11 (285%)	care than before admission
	monitoring unit (CMU)	-confirmed delirium dx	Dementia + delirium	22 (56%)	-mortality rate
Study Length/Start-	admission	-determined probable cause(s)	Other psych dx + delirium	6 (16%)	5
Stop Dates	n = 49 oncology	-made treatment recommendations	Initial recommendations	39 (100%) (investigations; drug	Patients in the treatmer
3 weeks	admission	-recorded findings and recommenda-		prescriptions; other; combination)	group without dementia
5 WEEKS	n = 196 geriatric		Compliance		<0.05) or with a specific
<b>.</b>		tions on the regular hospital consultation	Compliance	Range = 77% to 97%	
Purpose	services admission	form in patient chart			cause of delirium (p < 0.0
To determine whether	n = 47 language barrier	Follow up by a liaison nurse (see	Mortality	Treatment vs control	were more likely to impro
systematic detection	n = 22 discharge	"Nursing Intervention Protocol" Table 1 in		33% vs 37%	at 2 weeks.
and treatment of	n = 8 death	PDF)			
elderly medical	n = 33 combination of	-daily follow up for up to 8 weeks		N = 57 (all patients)	While the improvement in
npatients with	reasons	-confirm recommendations implemented		Treatment + control	CBGRS scores in the
delirium would reduce	n = 2 refusal	-consulted with patient's nurse(s)	SPMSQ and CGBRS	Initial scores were higher (patients	treatment group compare
				0 (1	to the control group was
cognitive impairment,	A	-checked with consultant if patient		more impaired) among those who	
abnormal behavior,	Assessment tools:	management problems		died that those who survived but NS	statistically significant, it
functional disability,	Confusion Assessment	-conducted weekly patient mental status			probably is clinically
use of restraints,	Method (CAM)	assessment	SPMSQ	Improved over time (<0.05)	relevant.
ength of hospital	Short Portable Mental		CGBRS	Improved marginally (<0.06)	
stay, need for	Status Questionnaire	Delirium reassessment by RA on weeks		Pattern of improvement did not	Excluding patients admitt
ncreased care after	(SPMSQ)	1, 2, 4, and 8		change when those who died were	to the geriatric department
discharge and rate of	Crichton Geriatric	1, <u>2</u> , 1, and 0		added to the analysis	may have had more
-	Behavioral Rating Scale	Follow up by BA as listed			5
death.		Follow up by RA as listed			treatable condition
	(CGBRS)			ot	
Funding source(s):		n = 46 control group	Delirium assessment:	See above RA 1 <sup>st</sup> assessment and	Patients who developed
St Mary's Hospital	Follow up by RA (data	n = 14 had a geriatrician/psychiatrist		at 1, 2, 4, and 8 weeks	delirium during their
Foundation	collection)	consultation during the study period			hospital stay (incident)
	1. Presence of initial	5 <b>, ,</b>	Baseline characteristics	No significant differences between	rather than those who we
Quality Score	consultation in patient	Men and women (58.7%)		patients who were and were not	delirious at admission
3	record	Mean age 85.4 (6.3)		referred for a geriatrician/	(prevalent) may have bee
	2. Use of restraints	Weat age 03.4 (0.3)			more treatable.
Diak of Diac		Hered was direct as we		psychiatrist consultation while	more treatable.
Risk of Bias:	3. Length of stay during	Usual medical care		receiving usual care (control)	
High	the study period	RA also collected	Outcomes		The characteristics of the
	<ol><li>Discharge information</li></ol>	-baseline assessment data	Delirium dx by attending	16%	enrolled patients (very ol
	(locationhomefacility)	-use of restraints			very ill, high mortality and
	Compliance with initial	-length of stay during study period			more than half with
	recommendations	-whether delirium had been detected by			dementia and delirium) n
	Dates of follow up, new	,			have reduced the effect of
	• •	the attending physician			
	recommendations,				the intervention.
	compliance	Attending/clinical staff could request a			
		geriatrician or geriatric psychiatrist			
		consultation			

more likely to respond or by intervening more intensively,

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Unclear	More women in treatment group
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	35% deaths
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	Unclear	Some outcomes = 57 (treatment + control); some = 88 all enrolled
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		<50 each group
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

## G5-Cole MG, McCusker J, Bellavance F, et al. Systematic detection and multidisciplinary care of delirium in older medical inpatients: a randomized trial. CMAJ. 2002;167(7):753-9.

Canada Setting 5 medical units – University Hospital Study Design randomized trial	Population N = 5216 age ≥65 admitted to medical units n = 3291 excluded (see below) n = 1925 eligible for screening N = 299 prevalent or incident delirium n = 72 did not consent N = 207 medemined	Intervention Groups n = 113 Intervention group n = 110 received intervention n = 7 withdrawn n = 106 completed trial Men and women (58.4%)	Measure Delirium assessment: CAM SPMSQ (dx DSM III R)	Outcome Screened at admission by SPMSQ and CAM by nurses for prevalent delirium and 1 week later for	Comments Changes from prior study:
Cole MG 2002 Canada Setting 5 medical units – University Hospital Study Design randomized trial	<pre>medical units n = 3291 excluded (see below) n = 1925 eligible for screening N = 299 prevalent or incident delirium n = 72 did not consent</pre>	n = 110 received intervention n = 7 withdrawn n = 106 completed trial Men and women (58.4%)	CAM	and CAM by nurses for prevalent	
Canada Setting 5 medical units – University Hospital Study Design randomized trial	<pre>medical units n = 3291 excluded (see below) n = 1925 eligible for screening N = 299 prevalent or incident delirium n = 72 did not consent</pre>	n = 110 received intervention n = 7 withdrawn n = 106 completed trial Men and women (58.4%)		and CAM by nurses for prevalent	
Setting 5 medical units – University Hospital Study Design randomized trial	n = 1925 eligible for screening N = 299 prevalent or incident delirium n = 72 did not consent	n = 106 completed trial Men and women (58.4%)	SPMSQ (dx DSM III R)	dolirium and 1 wook later for	
5 medical units – University Hospital <b>Study Design</b> randomized trial	N = 299 prevalent or incident delirium n = 72 did not consent	Men and women (58.4%)		delinuni and i week later for	-more intensive
Hospital Study Design randomized trial	<b>delirium</b> n = 72 did not consent			incident delirium before	-consultant followed
Study Design randomized trial	n = 72 did not consent			randomization; CAME and MMSE	patients
Study Design randomized trial				inter-rater reliability "excellent"	-study nurse visited 5 x
randomized trial		Mean age 82.7 (7.5)			week
			Baseline characteristics	No significant difference between	-study team (2 geriatric
	N = 227 randomized	Study nurse not blinded to		groups	internists, 2 geriatric
	N = 113 intervention	intervention			psychiatrists, study nurse)
	N = 114 usual care		Primary outcomes	Intervention vs usual care	met to discuss delirium
Computer generated random		<ol> <li>Consultation and follow up by</li> </ol>		No significant difference between	management problems
	Inclusion	geriatric internist or psychiatrist		groups for any outcome	-primary investigator met
	Age ≥65	-determine predisposing,			weekly with study nurse to
	Prevalent delirium at admission	precipitating and perpetuating	Prevalent delirium	80.5% vs 80.7%	discuss dx, enrollment,
	Incident delirium within 1 week	factors of delirium	NS risk if prevalent	1.15 (0.48-2.79)	interventions.
	Informed consent by patient or	-made management	Incident delirium	19.5% vs 19.3%	
	decision maker	recommendations			There were no deviations
Study Length/Start-Stop			Delirium + dementia	59.3% vs 56.1%	from the planned study
	Exclusion	<ol><li>Follow up by study nurse</li></ol>	NS for delirium + no		protocol
	N = 3291	-daily visit (mean 35.7 min)	dementia	HR 1.54 (0.82-2.97)	
	n = 362 stroke	-assure implementation of			Delirium may be an
	n = 326 language barrier	recommendations	Improvement in MMSE	48% vs 45%	epiphenomenon related to
	n = 117 not Montreal resident	-assure nursing protocol	score		the severity of medical
	n = 209 >48 h in ICU	implementation (see Table 1 in			illness; consequently the
	n =310 in CMU	PDF)	Severity of illness score	5.8 (1.2) vs 5.8 (1.3)	psychosocial component
	n = 640 oncology admission	<ul> <li>meet with/involve patient family</li> </ul>	Charlson comorbidity index	3.2 (2.2) vs 3.3 (2.1)	of the intervention may
	n = 337 geriatrics admission		NS for less comorbidity	HR 1.36 (0.75-2.46)	have been superfluous
	n = 460 long term care unit				
	n =82 discharged		Time to improvement	NS trend toward shorter time for	In the absence of an
	n = 29 died			intervention group	effective intervention
	n = 116 previously enrolled			48% vs 45%	strategy for prevalent or
	n = 92 communication problem			HR 1.10 (0.74-1.63)	incident delirium in older
	n = 155 refused screening		Delirium Index Score	8.34 (3.87) vs 7.36 (3.49)	patients, research efforts
	n = 56 other reason			HR 1.09 (0.74-1.60)	should focus on prevention
rate of discharge to the				The second state of the set of the second state is	of delirium in this
community. Also to improve				The results of the efficacy analysis	population.
	All patients assessment			did not differ from the main analysis	This might invelve
· · · · ·	Blinded RA within 24H: Baseline MMSE		Dellation and a second sector	On a share	This might involve
iongaio or otaly and improvo		n = 114 Usual care group	Delirium assessment:	See above	identification of potentially
	Delirium Index Barthel Index	n = 114 received yusual care n = 2 withdrawn	Descling characteristics	Cas shave	modifiable predisposing or precipitating risk factors for
	Collected demographic and		Baseline characteristics	See above	prevalent delirium and
	clinical (chart) information	n = 112 completed trial		See above	evaluation of interventions
	Family interview:	Man and waman (E0%)	Primary outcomes	See above	aimed at risk factor
Grant - National Health	Informant Questionnaire on	Men and women (50%)			abatement.
	Cognitive Decline in the Elderly	Mean age 82.0 (7.1)			abatement.
Program of Health Canada.	Cognitive Decline in the Eldelly	Usual care			
	Follow up	-standard hospital services			
	RA yusing process of care				
	checklist	-consultation requests honored			
	Chart review by nurse	-no systematic follow up by			
	abstractor (Charlson	geriatric specialists or nurse if			
		consultation provided			
	comorbidity index	-dx of delirium not provided to hospital staff			
		ทบรุ่มเล่า รเล่า			
Conclusion: Systematic data di	on and multidioniclinear area of the	inium dooo not onnearte he mare he	noficial than yourst same fact at the	r patients admitted to medical services.	101

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Study nurse not blinded
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Study nurse not blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
<ul> <li>8. Sample size ≥50 each study arm (1 point if achieved):</li> </ul>	1		
	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G5-Mador JE, Giles L, Whitehead C, Crotty M. A randomized controlled trial of a behavior advisory service for hospitalized older patients with confusion. Int J Geriatr Psychiatry. 2004;19(9):858-63.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Mador JE 2004	N = 127 assessed for	n = 36 intervention	Delirium assessment:	Ongoing assessment not described	No patients were lost to
Australia	eligibility	n = 2 deceased	CAM at admission	5 5	follow up
	n = 56 excluded (see	n = 34 discharged			·
Settina	below)	······································	Baseline characteristics	Significant difference between	Data on deceased patient
2 Metropolitan Teaching	N = 71 randomized	Men and women (42%)	Bucchine characterietiee	groups	included in analysis (ITT)
Hospitals		Mean age 82.1 (80.0 – 84.3)		Intervention (36) vs control (35)	
lospitais	Inclusion	Prior residence = home 64%	Prior residence = home	64%  vs  86%,  p = 0.035	Possible reasons the
Study Design	Age ≥60	Current geriatrician = 61%	Current geriatric care	61% vs 29%, p = 0.006	intervention was ineffectiv
	Medical or surgical	Delirium only 6%	Current genatic care		-EPN advice may not off
RCT	0			No other significant differences	5
	inpatient	Dementia only 50%		between groups at baseline	an advantage over medic
Randomization method	Confused due to	Delirium + dementia 44%	<b>.</b>		advice from a geriatrician
Pharmacy department in	-dementia (DSM-IV)		Primary outcomes	Intervention (36) vs control (35)	care nursing staff are
one of the study hospitals	-delirium (CAM)	Patients referred to the Extended	PAS	1.7 (0.4) vs 1,.8 (0.3) NS (p = 0.369)	already providing
by person external to the	-combination	Practice Nurse (EPN) in aged care	PAS subgroup analysis	n = 12 vs 17	-adherence to EPN advi
study) in blocks of 10	Behavioral disturbance that	<ul> <li>Seen by the EPN within 24h of</li> </ul>	Initial PAS ≥4	NS (p = 0.713)	not measured
stratified for the 2 hospitals	was problematic to ward	randomization	Sleep	NS (p = 0.212)	-may have been more
computer generated table	staff	-assessed patient	Restraint use	NS OR 0.42(0.07-2.51), p = 0.345	effectively delivered by a
of random numbers)	Informed consent by family	-formulated management plan	MAI	NS (p = 0.061)	multidisciplinary team
	member	(non-pharm)	Doses of antipsychotics	NS (p = 0.817)	-patients cared for on
Study Length/Start-Stop		-discussed plan with ward nurses	Doses of benzodiazepines	NS (0.730)	same ward so nurses ma
Dates	Exclusion	-provided ongoing support and		, , , , , , , , , , , , , , , , , , ,	have delivered useful
0/2002-8/2003	N = 56	education to nursing staff	Secondary outcomes		strategies to control group
	n = 16 presence of primary	Non-pharm plan	Length of stay	NS (p = 0.557)	-patients may not have
Purpose	psychiatric illness	-tailored to patient needs	Faller status	NS ( $p = 0.083$ )	been agitated enough at
To determine whether	(responsible for behavioral	-addressed safety issues	Nursing satisfaction	NS ( $p = 0.497$ )	baseline to show significa
ndividualized advice on	disturbance)	-close supervision	Next of kin satisfaction	NS (p=0.488)	improvement
non-pharmacological	n = 5 absence of next of	-minimized restraint use	Discharged to residential	140 (p=0.400)	-study may have been
strategies for hospitalized	kin to consent	-reduced falls risk	care (if admitted from		under powered
older patients with	n = 17 no behavioral	-communication with patient	•	NS (0.577)	under powered
•	problem	-communication with patient	home)	NS (0.577)	
confusion and behavioral	• • • •				
problems can improve	n = 5 confusion resolved	-targeted behavioral strategies			
evels of agitation and	n = 7  age  < 60	-education for nursing staff			
reduce the use of	n = 3 next of kin refused	(reframing behavior and triggers)			
osychotropic medication.	n = 3 missed (not				-
	randomized)	n = 35 control	Delirium assessment:	See above	
Funding source(s):		n = 2 deceased			
Medical Benefits Fund of	Trial period	n = 33 discharged	Baseline characteristics	See above	
Australia Health Research	Time of randomization until				
Award and the Department	the time of discharge or the	Men and women (54%)	Primary outcomes	See above	
of Veteran Affairs, Australia	date on which the patient	Mean age 82.9 (81,4-84.5)			
	was approved for	Prior residence = home 86%	Secondary outcomes	See above	
Quality Score	discharge to a residential	Current geriatrician = 29%	-		
4	care facility	Delirium only 9%			
	-	Dementia only 54%			
Risk of Bias:	Assessment tools	Delirium + dementia 37%			
High	Pittsburgh Agitation Scale				
	(PAS)				
	Medication	Usual care by a geriatrician for			
	Appropriateness Index	medical advice of the patient's			
	(MAI)	confusion and behavioral disturbance			
	. ,	contrusion and benavioral disturbance			
	Total daily doses of				
	benzodiazepines and				
	antipsychotics				

and behavioral problems in an acute hospital.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences between groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Blinding for some outcomes but clinicians not blinded
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Significant baseline imbalances (ITT analysis done)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		? only for initial assessment
8. Sample size ≥50 each study arm (1 point if achieved):	0		<50 each group
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G5-Marcantonio ER, Bergmann MA, Kiely DK, Orav EJ, Jones RN. Randomized trial of a delirium abatement program for postacute skilled nursing facilities. J Am Geriatr Soc. 2010;58(6):1019-26.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	Other functions associated with the study
MarcantonioER 2010;	N = 457 enrolled (consent)	n = 282 Delirium Abatement	Delirium assessment:	Eligibility assessment: Trained	Administrative
JSA	n = 282 DAP	Program	CAM	researches completed a structured	Advisory Council
	n = 175 usual care	-	MMSE	interview within 5 days of admission	(AAP) (Facilities)
Setting		Men and women (61%)	DSI	using CAM, MMSE, Digit Span and	-administrative leader
Multicenter (8)	NOTE: See detailed	Mean age 83.8 (7.4))	Digit Span	DSI	-nursing leaders
Skilled nursing facilities	CONSORT flow chart (PDF p			Ongoing assessments by trained RAs	-medical leaders
Study Design	1022) for facility inclusions/ exclusions and patient	Nursing implementation of DAP		(blinded) using the CAM algorithm	Met every 3 months at DAP sites; every 6
Cluster RCT	inclusions/exclusions	-Long-term Care Resident Assessment Instrument (v2)	Baseline characteristics	Significant difference between groups <b>DAP vs usual care</b>	months at usual care sites
Randomization method	Inclusion (facilities)	-nurses blinded to results of		96% vs 84%, p <.01	
After matching on	Boston-area skilled nursing	RA eligibility assessments		46% vs 32%, p <.01	AAP Role
ownership status, size,	facilities	-all nurses educated (CME	White race		Reviewed processes
and setting (urban vs suburban) facilities	≥ 35 PAC admissions/ month Facility leadership supported	based pre and post testing) -DAP facilities received the	Clinical dementia	DAP adherence (n = 282)	<ul> <li>-patient screening</li> <li>-consent</li> </ul>
andomized to DAP or	study participation	eligibility assessment materials	Primary outcomes	75%	-follow up
usual care (patient	Minimum threshold for quality	(not results)	DAP structured delirium	41%	-adherence at DAP
andomization based on	of care based on state survey	-environmental modifications	assessment	38%	sites
acility)	results	provided	Delirium triggered in med record	33%	
	Inclusion (patients)	-5 measures of DAP	Assessment of causes completed		DAP sites
Study Length/Start-	Age ≥65	implementation developed and	Nursing care plan completed	35%	-introductory letter to
Stop Dates	Admitted directly from an acute	monitored quarterly	Environmental modifications	DAP vs usual care	physicians and nurse
0/2000-12/2003	medical or surgical	-tip sheets provided to assist	performed	41% vs 12 %, p <.001	practitioners
Purpose	hospitalization	with implementation		The majority of cases remained	-semiannual
To determine whether a	English speaking	-Delirium Resource Nurse	Detection of delirium	undetected at all facilities	newsletter to update
delirium abatement	Able to communicate before	identified and given extra			personnel
program (DAP) can	acute illness	training		There was little evidence to suggest	<ul> <li>highlighted importar</li> </ul>
shorten duration of	Life expectancy >6 mo	-Assessment of Causes form		that more interventions were	aspects of delirium
delirium in new	Lived within 2,5 miles of	-delirium nursing care plan		performed at DAP than at usual care	detection and
admissions to postacute care (PAC)	research site	-at least 2 environmental modifications placed in each		sites	management
	Exclusion	patient's room		No difference between groups	Delirium Managemei
Funding source(s):	N = See detail in CONSORT	-DAP facilities received small	Persistence of delirium	At 2 weeks (67.8% vs 65.7%, p = .77)	Trained nurse
National Institute on	chart (p 1022 in PDF)	incentive payments based on		At 1 month (59.9% vs 509.7%, p = .48)	conducted identical
Aging Grant and Paul	End stage dementia	performance (up to \$700 every	Rates of death	No difference between groups	reviews of DAP and
Beeson Physician	Complete functional	6 months)		At 2 weeks (2.1% vs 2.3%, p = .89)	usual care sites'
aculty Scholar in Aging	dependence before			At 1 month (8.5% vs 9.1%, p = .78)	medical records to
Research	hospitalization				identify important
	Refused (patient or caregiver)	n = 172 usual care	Delirium assessment:	See above	processes:
Quality Score					-documentation, by
4 Risk of Bias:	Eligibility Study personnel screened all	Men and women (69%) Mean age 84.4 (7.2))	Baseline characteristics	See above	physicians/nurse practitioners
Unclear	new PAC admissions for trial eligibility (delirium assessment)	Usual care	Primary outcomes	See above	-evaluation and treatment for reversibl
	Proxy interviews to obtain		Secondary outcomes	See above	causes
	information associated with		-		-prevention and
	-Charlson scale				management of
	-pre-hospitalization self care				common complication
	function (for ADLs)				-restoration of function
	-DSM IV criteria for dementia				
	-reviewed medical records for				
	dx codes	1			

105

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Patient significant differences at baseline
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	Unclear	No detail provided on how randomization was performed
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	DAP facilities aware of intervention status
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Multivariate analysis using baseline imbalances did not change outcome data All patients included in outcomes but not specific ITT design
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G5-Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. Multicomponent geriatric intervention for elderly inpatients with delirium: a randomized, controlled trial. J Gerontol A Biol Sci Med Sci. 2006;61(2):176-81.

Study	Dopulation	Intervention Groups		Results	Commonte
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments
Pitkala KH 2006	N = 2040 admitted (>69 yr)	n = 87 intervention	Delirium assessment:	Admission screen by 2 trained study	Systematic methods on
Finland	n = 350 not eligible for	n = 87 follow up 3 & 6 months	CAM	nurses following standardized	screening or preventing
	screening		MMSE	procedures using CAM and MMSE;	delirium are not used in
Setting	N = 1690 screened	Men and women (75.9%)	Digit Span	positive CAM assessed by study	the study hospital
•			DSM IV	physician; delirium dx confirmed by	the study hospital
General medicine units	N = 379 CAM positive	Mean age 83.8 (5.6)			
(6) City Hospital	n = 205 excluded		Memorial Delirium Assessment	DSM IV criteria. Daily MDAS during	This intervention did not
	N = 174 met DSM IV criteria	1. Accurate dx of delirium	Scale (MDAS)	first week in hospital and every second	improve patients' gener
Study Design	n = 87 intervention	2. Comprehensive geriatric		day thereafter	prognosis as indicated
RCT	n = 87 control	assessment			no effect on mortality,
		3. Avoid conventional neuroleptics	Baseline characteristics	No significant differences between	institutionalization or
Randomization	Inclusion	in favor of atypical antipsychotics		groups	length of hospital stay
method	Age >69	4. Orientation		groupo	with delirium
	Informed consent from	5. Physiotherapy	Primary outcomes	Significant difference in treatment	with definant
Computer generated			Primary outcomes		In the same of full blows
andom numbers	closest proxy	6. General geriatric interventions		interventions % vs %, p	In the case of full blown
assigned consecutively		-nutritional supplements		Intervention (87) vs Control (87)	delirium, this type of
by blinded staff	Exclusion	-calcium + vitamin D	Atypical antipsychotics	69.0% vs 29.9%. p <.001	intervention may be "too
member	N = (see below)	-hip protectors	Conventional neuroleptics	8.0% vs 23,.0%, p = .006	little too late" to produce
	Not screened (305)	7. Cholinesterase inhibitors if	Acetylcholinesterase inhibitors	58.5% vs 9.3%, p <.001	a significant difference
Study Length/Start-	n = 118 admission from	MMSE <23	Vitamin D + calcium	77.0% vs 9.3%, p <.001	prognosis and thus, eve
Stop Dates	permanent institutional care	-also MRI or CT if cognition	Nutritional supplements	92.0% vs 0.0%, p <.001	more effort should be
9/2001-11/2002	facility	impaired after delirium resolution	Hip protectors	90.8% vs 1.1%, p <.001	focused on prevention
9/2001-11/2002			The protectors		
_	n = 202 discharged <48 h	8. Comprehensive discharge	Physical therapy	89.7% vs 44.8%, p <.001	delirium among such
Purpose	n = 30 refused screening	planning	Specialist consultations	49.4% vs 28.7%, p = .005	patients.
To investigate whether	Screened/excluded	-consultation with social worker	CT or MRI scans	51.7% vs 8.0%, p <.001	
a comprehensive	n = 23 refused	<ul> <li>occupational therapist home</li> </ul>	Intensity and severity of		Post hoc analysis of
geriatric assessment	n = 24 terminal prognosis	visit	delirium symptoms improved at		patient and intervention
and individually tailored	n = 4 discharged before	-discharge planning with	6 months (MMSE score)	18.4 vs 15.8, p = 0.047	factors impacting
treatment are effective	delirium dx confirmed	caregiver(s)			prognosis:
in reducing mortality	n = 10 permanent institutional	ca.cg.rc.(c)		No significant difference between	-Barthel Index score
and permanent	care			groups	significant for mortality
			Delivium deux (maan, CD)		
institutional care among	n = 15 no caregiver/consent		Delirium days (mean, SD)	29.3 (25.6) vs 22.4 (18,.4), p = .171	HR 2.1 (1.1-4.0)
patients with delirium.	n = 129 did not meet DSM IV		Deceased	34.5% vs 29.9%, p = .516	-nutritional supplemen
Also to determine	criteria		Admitted to permanent		protected against death
whether this treatment			institutional care	42.5% vs 51.7%, p = .224	HR 0.3 (0.1-0.8)
is beneficial in reducing	All patients protocol				
the number of days	Screened within 2 days of	n = 87 control	Delirium assessment:		Antipsychotics and ChE
spent in institutions,	admission (baseline)	n = 83 follow up 3 & 6 months			did not affect mortality
alleviating delirium, or	-CAM, MMSE, Digit Span	n = 4 refused assessments but	Baseline characteristics		and not anoot monality
			Dasenne characteristics		
mproving cognition or	-proxy interview	allowed medical record retrieval of			
physical functioning of	-premorbid dementia	endpoint data	Primary outcomes		
these patients.	status (CDRS; DSM IV)				
	-med record review	Men and women (71.3%)	Secondary outcomes		
Funding source(s):	<ul> <li>-comorbidities (CMI)</li> </ul>	Mean age 83.3 (6.2)			
Lions Organization,	Follow up at 3&7 6 months				
Helsinki University	-MMSE	Usual care			
Central Hospital,	-Barthel Index				
Academy of Finland	-IADL scale				
including of Filliand	-Geriatric Depression Scale				
Quality Coores 7					
Quality Score: 7	-Mini-Nutritional				
	Assessment				
Risk of Bias: Unclear	-proxy interview				
				comprehensive geriatric treatment is justif	
		ved cognition. However, individual cas	ses deserve careful tailoring of trea	tment and evaluation whether they benefit	from active, curative
eatment or good palliativ	/e care.				107

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	No comment on blinded outcome assessment
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G5-Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet. 2009;373(9678):1874-82.

	Barrad fi	lateranti O		Results	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Schweickert WD 2009	N = 1163 patients screened	n = 49 intervention	Delirium assessment:	Daily independent neurological	Deaths before
USA	n = 343 excluded	No patients discontinued	CAM-ICU	assessments by non-blinded study	discharge (NS)
	N = 818 eligible for enrollment	protocol or lost to follow up	RASS	personnel using the RASS for level of	Intervention
Setting	n = 714 excluded			arousal and CAM-ICU for delirium and	N = 9 (18%)
Multicenter (2)	N = 104 randomized	Men and women (59%%)		coma (inter-rater reliability and severity not	Control
University hospitals	n = 49 intervention	Mean age (range) 57.7 (36.3-		discussed)	N = 14 (25%)
	n = 55 control	69.1)			
Study Design			Baseline characteristics	No significant difference between groups	Deaths before
RCT	Inclusion	Exercise and mobilization		nto organicant anterence between groupe	intervention
	Age ≥18	(physical and occupational	Primary outcomes	Significant differences between groups	N = 3
Randomization method	On mechanical ventilation <72	therapy)	Fillinary outcomes	Intervention (49) vs Control (55)	11 - 5
		Daily protocol	Magn dynation of DT OT	intervention (49) vs Control (55)	Discontinuation of
1:1 allocation by	h Maalaan isalaan tilatissa		Mean duration of PT, OT	0.00 (0.17.0.10)	Discontinuation of
computer generated	Mechanical ventilation	-sedatives interrupted	(hr/day)	0.32 (0.17-0.48) vs 0.0; p <0.0001	therapy due to patient
permuted blocks by	expected to continue >24 h	-unresponsive patients	Time from intubation to first		instability in 4% of all
consecutively numbered	Baseline functional	underwent passive range of	PT/OT session (d)	1.5 (1.0-2,.1) vs 7.4 (6.0-10.9); p <0.0001	sessions (most
sealed envelopes by	independence (Barthel score	motion exercise in all limbs	Return to functional status	59% vs 35%; p = 0.02 OR 2.7(1.2-6.1)	commonly for perceived
nvestigator with no	≥70 – obtained from proxy re	<ul> <li>-if patient able to interact,</li> </ul>	Time to functional milestones	P <0.001 for all (Table 4)	patient-ventilator
further involvement in	patient function 2 weeks	active assisted and/or active	ICU delirium (d)	2.0 (0.0-6.0) vs 4.0 (2.0-7.0) p = 0.03	asynchrony)
the study; assessment	before admission)	independent range of motion	Time in ICU with delirium $(\%)$	33% (0-58%) vs 57% (33-69%), p = 0.02	
therapists were different	,	exercises in the supine	Hospital days with delirium (d)	2.0 (0.0 -6.0) vs 4.0 (2.0-8.0), p = 0.02	Comments
than intervention	Exclusion	position		2.0 (0.0 0.0) V0 1.0 (2.0 0.0), p 0.02	Patients in the
therapists	N = see below	-as tolerated, treatment was		Variables associated with achievement	intervention group had a
literapists	Excluded at screening	advanced and bed mobility		of functional independence HR (CI), p	shorter duration of ICU-
Study Length/Start-	N = 343	,	4.70		
		activities initiated	Age	0.96 (.9498), p = 0.001	associated delirium by
Stop Dates	n = 1 aged < 18	-sitting balance activities	Absence if sepsis	2.26 (1.03-4.97), p = 0.04	2.0 days and spent 2-4
Not described	n 161 mechanical ventilation	followed by ADLs and	PT/OT intervention	1.84 (1.02-3.31), p = 0.04	more days alive and
	>72h	exercised that increased			breathing without
Purpose	n = 181 dependent prior	functional independence		No significant difference between	assistance than
To assess the efficacy of	functional status	-progressed to transfer		groups	controls.
combining daily	Excluded from enrollment	training and pre-gait exercises		-sedation and analgesia practice	
interruption of sedation	n = 150 no consent	-therapy continued daily until		-occurrence and duration of daily	Early physical and
with physical and	n = 173 extubation order	patient reached previous level		interruption of sedation	occupational therapy,
occupational therapy on	n = 122 cardiac arrest	of function or discharge		-proportion of time on mechanical	combined with daily
functional and	n = 126 irreversible condition			ventilation spent receiving sedative or	interruption, was safe
neuropsychiatric (such	(>50% 6 month mortality)			opiate	and well tolerated.
as ICU-associated	n = 103 rapidly developing			-high spontaneous breathing trial	
delirium) outcomes in	neurologic/neuromuscular			performance rates	Delirium and
,	disease			-reasons and occurrence rates for	neuromuscular function
patients receiving					
mechanical ventilation in	n = 30 conflicting study n = 5 advanced dementia			unsuccessful spontaneous breathing trials	are undoubtedly linked.
intensive care.				-ICU length of stay	
	n = 1 raised intracranial	n = 55 control			Without intact cognition,
Funding source(s):	pressure	No patients discontinued	Delirium assessment:	See above	physical activity is either
Identified as "none"	n = 6 multiple absent limbs	protocol or lost to follow up			self-limited or
No conflicts of interest	Enrollment in another trial		Baseline characteristics	See above	iatrogenically limited,
listed by authors		Men and women (42%)			cooperation with
-	All patients	Mean age (range) 54.4 (46.5-	Primary outcomes	See above	therapy is poor and any
Quality Score:	Goal directed sedation guided	66.4)	· • • • • • • • • • • • • • • • • • • •		immobilization injury is
6	by Richmond Agitation		Secondary outcomes	See above	likely exacerbated.
-	Sedation Scale (RASS)	Usual care (PT or OT only as			
Risk of Bias:	Protocol for weaning from	ordered by primary care team)			
		ordered by primary care team)			
Unclear	mechanical ventilation				
O - male al anno 1 - 1 - 1 - 1	and the last state of the second state of the	line al basistance d'arte de la dest			
				thing trials, and physical and occupational the	
				atients assigned to intervention had shorter du	
		an be achieved with the coordinate	ed efforts of multiple disciplines de	dicated to the survival and mental and physica	recovery of <sub>1</sub> هؤically ill ال
patients receiving mechani	adventilation				

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Delirium assessors not blinded
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved):         <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		<50 intervention group
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

**G1 G2-** Mouzopoulos G, Vasiliadis G, Lasanianos N, et. el., Fascia iliaca block prophylaxis for hip fracture patients at risk for delirium: a randomized placebo-controlled study, J Orthop Traumatol. 2009; 10(3):127-33.

Study	Population	Intervention Groups	Measure	Sults Outcome	Adverse
Characteristics	•		เพเซสวินเซ		Effects/Comments
Nouzopoulos G 2009	N = 324 admitted to	n = 108 FICB group	Delirium assessment:	Daily assessments by	
Greece	orthopedic department	Dropouts	CAM	experienced nurses and	There were no
	N = 37 excluded before	n=1 died	DRS-R-98	geriatricians based on a	complications of
Setting	screening	n=3 denied participation	Digit span - attention	structured multimodal protocol	FICB administration
npatients in orthopedic	N = 287 screened	n=2 lost at follow-up	DSM-IV	including delirium assessment	except three local
vard	n = 53 low delirium risk	n = 102 analyzed	Domit	and severity if diagnosed; specific	hematomas
		Intermediate Risk = 85		training and inter-rater reliability	developed at the
Study Decian	N = 210 randomized			not discussed	
Study Design	N = 219 randomized	High Risk =17		not discussed	injection site, which
RCT -placebo-controlled,	n = 108 FICB	Age (years) = $72.3 \pm 4.1$			resolved
	n = 111 placebo	Men and Women (23.5%)	Baseline characteristics	No significant difference between	spontaneously.
Randomization method		APACHE II score = $12.89 \pm 2.13$		groups	- · ·
Orthopedic surgeons,	Inclusion	MMSE score = $24.1 \pm 3.6$	Patients who developed	No significant difference between	Comments
neurologists and nurses	Age ≥70 years	Visual acuity = $0.4 \pm 0.12$	delirium	groups	No significant
dentified potentially eligible	Admitted for hip fractures	Dehydration index = 20.15 ± 3.47			difference between
patients by systematically				FICB v placebo group	groups in use of pa
creening new admissions	Exclusion	Intervention	Primary outcomes	N = 102 vs 105	medication and no
o one orthopedic ward;	N= 37 (not screened)	0.25 mg bupivacaine on admission and	Incidence of delirium		correlation with
patients with intermediate	13 Refused to participate	every 24 h until delirium occurrence or	All patients	11(10.8%) v 25 (23.8%)	development of
or high risk of delirium were	11 taking antipsychotic drugs	surgery. 24 h post-op FICB was re-	Relative risk OR (CI)	0.45 (0.23 to 0.87)	delirium
sequentially randomized to	4 = Parkinsonism	administered and repeated daily every	High risk patients	9/17 v 10/16	aointain
reatment or placebo using	4 = pathologic hip fracture	24 h until delirium or discharge. A	Relative risk OR (CI)	0.84 (0.47 to 1.52)	No significant
a computer generated	(metastasis)	standardized FICB technique was used	Intermediate risk patients	2/85 v 15/89	difference between
	2 = acute MI at admission				
code; all participants		for the patients.	Relative risk OR (CI)	0.13 (0.03 to 0.53)	groups for delirium
blinded to study group	2 = delirium at admission	Pain was treated with paracetamol (1			for patients classif
allocation	Baseline exclusions	g/6.7 ml) and pethidine (50 mg) as	Secondary outcomes		as high risk, but the
	13 = refused study drug tx	needed	Severity of delirium		was a significant ris
Study Length/Start-Stop	2 = died before study started		DRS-R-98 highest value	14.34±3.6 v 18.61±3.4,	reduction for FICB
Dates	53 = low risk		Mean difference (CI)	4.27 (1.8 to 5.64) p <0.001	patients classified a
07/2004-03/2008			Delirium duration (days (CI))	5.22 ± 4.28 v 10.97 ± 7.16 (3.87	intermediate risk (p
				to 7.62) p <0.001	not provided)
Purpose	Screening Risk Factors			<i>,</i> , ,	. ,
o assess the	Severity of illness	n = 111 placebo group	Delirium assessment:	See above	Although the study
effectiveness of fascia	-acute physiology	n= 2 died			controlled for
liaca compartment block	-age	n= 4 lost to follow-up	Baseline characteristics	See above	perioperative risk
FICB) for prevention of	-chronic health exam	n = 105 analyzed	Dasenne characterístics		factors it did not
perioperative delirium in hip	Cognitive impairment (MMSE)	Intermediate Risk = 89	Drimony outcomes	See above	examine the impact
			Primary outcomes	See above	
surgery patients who were	Index of dehydration	High risk = $16$			of drugs other than
at intermediate or high risk	Visual impairment	Age (years) = $73.1 \pm 3.8$	Secondary outcomes	See above	paracetamol and
or this complication.		Men and Women (22.4%)			pethidine,
	Definition of Risk	APACHE II score = $12.97 \pm 1.82$			
Funding source(s):	Intermediate risk = 1 or 2 risk	MMSE score = $24.43 \pm 3.2$			
Not disclosed	factors present	Visual acuity = $0.42 \pm 0.08$			
	High risk = 3 or more risk	Dehydration index = $20.24 \pm 3.15$			
Quality Score	factors present				
ł	-	Intervention			
		Placebo medication (water for injection)			
Risk of Bias:		was identical in appearance to the			
ligh		active drug and was administered			
		identically as the FICB was injected.			
		Intramuscular analgesics were			
		administered as needed in both groups.			
		paracetamol (1 g/6.7 ml) and pethidine			
		(50 mg) for pain as needed			

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not clear if outcome assessors were blinded; only patients
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Dropouts after randomization not included in analysis
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	Unclear	Incidence p values not included and dropouts were excluded from analysis
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT analysis Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G2-Kinjo S, Lim E, Sands LP, et al. Does using a femoral nerve block for total knee replacement decrease postoperative delirium? . BMC Anesthesiol. 2012;12 (4):2253-9.

Study Characteristics	Population	Intervention Groups	Measure	Outcome	
		•			Adverse Effects
Kinjo 2012	N = 88	n = 31 continuous femoral nerve	Delirium assessment:	On postop days 1-2, the same	Comments:
USA	n = 3 excluded (see below)	block	Confusion Assessment	trained RA conducted structured	
			Method (CAM)	interviews daily, that included the	This study showed
	N = 85 in analysis	Men 13 (42%)		CAM, NRS (pain), use of pain	femoral nerve block
University Hospital	n=14 drop out	Mean age 72.8 ± 5.8		meds, sleep-wake cycle and post-	reduced the rate of
	The 14 patients with incomplete	White: 23 (74%)		op benzodiazepine use; delirium	delirium. The current
	delirium assessment or preoperative	Less than college 12 (40%)		severity were not discussed.	findings did show that
prospective cohort	TICS score due to patients refusal or	College or above 18 (60%)			the use of femoral
study	medical condition. There was no	History of CNS disorders 18 (58%)	Deceline changeteristics	Formanal Black + BCA (24) va	nerve block reduced the amount of
Soloction mothod	significant difference between patients with missing vs without	Continuous femoral nerve block ±	Baseline characteristics	Femoral Block + PCA (31) vs PCA only (54)	
	missing data in all in all variables	patient controlled analgesia		No significant difference between	intraoperative opioid dose, but the opioid
femoral nerve block	missing data in all in all variables	patient controlled analgesia		groups except:	sparing effect did not
lemoral herve block	Inclusion	Received either general anesthesia	ASA >3	23 (74%) vs 25 (46%), p=0.01	appear to extend to
Study Length/Start-	>65 yrs	with inhalational agents or spinal	A3A 23	23 (7478) VS 23 (4078), p=0.01	the postoperative
Stop Dates	Surgery for unilateral total knee	anesthesia with single shot femoral			opioid. The reduced
2001-2011	replacement (TKR)	nerve block with local anesthetic	Primary outcomes		intraoperative opioid
	Informed consent	(e.g., 30 ml of 0.5% ropivacaine)	Delirium on POD1 or POD2	7 (25%) vs 31 (61%), p= 0.002	use is likely related to
Purpose		followed by continuous local		· () · · · · · (• · /•), p · • · • • •	the bolus of local
To compare the	Exclusion	anesthetic infusion in the femoral	Predictive variables for		anesthetic
incidence of post-	n = 3	nerve catheter	postoperative delirium		administered for
operative delirium	2 postoperative epidural infusion		, Pain management	OR 7.02 (2.06-23.97), p = 0.002	femoral nerve block
between patients who	1 femoral and sciatic nerve blocks	The anesthesia team performed	Preoperative TICS score	OR 0.87 (0.77-0,98), p = 0.03	during the catheter
had femoral nerve	Not able to speak English	sensory and motor testing of the	·		placement.
block for post-	No written informed consent	femoral nerve block immediately	Secondary outcomes		
operative analgesia	Moderate to severe dementia	before surgery	Length of hospital stay	5.7 ± 6.4 vs 5.0 ± 1.9 , p=0.58	Pain assessment was
vs. those who did not.	Postop epidural catheter		Altered sleep-wake cycle d1	10 (33%) vs 25 (49%), p= 0.17	conducted once daily
			Pain at rest on POD 1	4.6 ± 3.0 vs 4.5 ± 2.9, p= 0.89	during the patient
Funding source(s):	Population selection source (s)		Change in pain level POD 1	0.9 ± 3.2 vs 1.9 ± 3.7, p= 0.20	interview. Because
NIH Grant	Part of a larger study examining the		Benzodiazepine use on POD 1	2 (6%) vs 9 (17%), p= 0.18	acute postoperative
[5RO1AG31795-03]	pathophysiology of postoperative		Hydromorphone dose d1	4.3 ± 4.6 vs 5.9 ± 6.1, p= 0.24	pain is dynamic and
	delirium conducted from 2001-2011				may fluctuate, we
Quality Score	at the UC San Francisco Med Ctr.		Dellahara esta esta esta	O a a ab a a	may not have
3	Preoperative assessment (all	n = 54 patient-controlled analgesia	Delirium assessment:	See above	evaluated the
Risk of Bias:	patients):	(PCA)	Baseline characteristics	See above	complex relationship between
High	(Anesthesia clinic <2 weeks before	Men 23 (43%)	Baseline characteristics	See above	postoperative pain
	surgery by a trained RA who also	Mean age 74.5 $\pm$ 6.5	Primary outcomes	See above	and delirium
	conducted postoperative	White: 39 (72%)	Finally outcomes	See above	completely.
	assessments)	Less than college 29 (56%)	Secondary outcomes	See above	completely.
	Interview (baseline demographics)	College or above 23 (44%)	Secondary Succomes		
	Hx CNS disorders	History of CNS disorders 35 (67%)			
	Daily alcohol consumption				
	Physical exam	PCA analgesia only			
	Use of benzodiazepines				
	Use of opioids	Received general or regional block			
	Preoperative pain level	(spinal or epidural) followed by			
	-Numeric Rating Scales (NRS)	intravenous PCA analgesia. The			
	Cognitive status (by telephone)	epidural catheter was discontinued in			
	-Telephone Interview for	the Post Anesthesia Care Unit			
	Geriatric Depression Scale (GDS)	(PACU) before the patient was			
		transferred to the floor.			1

**Conclusion**: Femoral nerve block reduces the incidence of postoperative delirium. These results suggest that a larger randomized control trial is necessary to confirm these preliminary findings.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	more patients classified as ASA>3 in the femoral nerve block group
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA – observational study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Drop out 14/85 >10%; dropouts analyzed with included patients, but 3 excluded patients not analyzed
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G4- Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. Anesthesiology. 2012;116(5):987-97.

				ults	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Hakim 2012	N = 101	n = 51 risperidone 0.5 mg q12h	Delirium assessment:	If ICDSC >3, psychiatrist	Risperidone vs Placebo
Egypt	n = 51 intervention	po.	Statistical Manual of Mental	confirmed delirium using DSM	Extrapyramidal:
	n = 50	-	Disorders (DSM)	criteria	2 (3.9%) vs 1 (2%); P=1.0
Setting	Inclusion	Men/women = 33/18		no inter-rater reliability, no	Death:
University hospital	>65 yr	Age: 65 to 70 yr 36 (70.6%)		cognitive testing done, no other	2 (3.9%) vs 1 (2%)
	Undergoing on-pump cardiac	>70 yr 15 (29.4%)		details described.	Mechanical ventilation:
Study Design	surgery	Intervention	SSD assessment:	See population column	3 (5.9%) vs 2 (4%)
A randomized,	No history of neuropsychiatric	The test drugs were continued for			Second operation:
double-blind, placebo-	disorders, alcoholism,	24 h after subsidence of SSD (0 on	Provide baseline		1 (1.96%) vs 2 (4%)
controlled, parallel-	substance abuse, or intake of	the ICDSC) or until ICDSC >3.	zharacteristics/measures	Risperidone vs Placebo	Abnormality of the QTc
arm study	psychotropic medications.	Patients who experienced delirium,	Demographic and Pre-op Data	No significant difference	interval and emergency
-	With SSD (ICDSC 1-3)	the dose of risperidone was	- MMSE score (28-30)	30 (58.8%) vs 31 (62%)	breaking of the
Randomization		incrementally increased until	- MMSE score (25-27)	21 (41.2%) vs 19 (38%)	concealment envelopes
method	Exclusion	symptoms were controlled or	-GDS (0-2)	25 (49%) vs 26 (52%)	0 vs 0
Randomization was	N= 142	attained dose of 4 mg/d.	-GDS (3-4)	26 (51%) vs 24 (48%)	
carried out by a	19 Declined to participate	Ģ	Operative and Post-op Data	No significant difference	Comments:
clinical pharmacist	47 Not meeting inclusion criteria	n = 50 placebo q12h po.	-post-op intubation >24 h	5 (9.8%) vs 3 (6%)	The current study showed
using a computer-	76 Not meeting criteria for SSD		ICDSC score 1	19 (37.3%) vs 17 (34%)	that 57.1% of patients
generated random	Exclusion criteria:	Men/women = 36/14	ICDSC score 2	17 (33.3%) vs 17 (34%)	experienced SSD after
number list created	MMSE<25	Age: 65 to 70 yr 39 (78%)	ICDSC score 3	15 (29.4%) vs 16 (32%)	surgery. The incidence of
with GraphPad	GDS >4	>70 yr 11 (22%)			clinical delirium observed
StatMate v.1.01i	Impaired hearing or visual acuity		Primary outcomes:		in the current study was
software using	Speech difficulty	Intervention (see above)	Possibly delirious: ICDSC >3	8 (15.7%) vs 19 (38%), p =.011	23.8%.
permuted blocks of	Contraindication to risperidone	Patients in the placebo group who	Incidence of delirium (DSM)	7 (13.7%) vs 17 (34%), p =.031	
size 4.	or haloperidol	experienced delirium were given	Absolute risk reduction	0.20 (95% CI, 0.04 – 0.37)	Neither the ICDSC nor the
Study Length/Start-	Hx of neuroleptic malignant	0.5 mg oral risperidone every 12 h,	Number needed to treat	4.9 (95% CI, 2.7–24.4)	CAM-ICU has been
Stop Dates	syndrome,	and if symptoms were not			validated for severity
12/2007 – 11/2010	Prolonged QTc syndrome	controlled, the dose could be	Secondary outcomes:		scoring of delirium, so the
	Hx cerebrovascular disease	increased to 4 mg/d.	Duration of delirium	3 (2 to 4) vs 3 (3 to 4) p=.664	highest score on the
Purpose	other noncardiac procedures	5	Need for haloperidol	2 (28.6%) vs 3 (17.6%) p=.608	ICDSC was reported in the
To evaluate the effect		In either group, haloperidol was	Highest doses of risperidone	3 (2 to 4) vs 3 (2.25 to 3.5) p=.318	current study as a
of treating	Assessment of SSD:	used as a second line rescue	Highest doses haloperidol	0 (0 to 1.5) vs 0 (0 to 0) p=.757	measure of severity,
subsyndromal	Screening SSD using the	medication if symptoms were not	Highest score on the ICDSC	6 (5 to 7) vs 5 (4 to 5) p=.234	taking advantage of the
delirium (SSD) with	Intensive Care Delirium	controlled with risperidone in a	Length of ICU	2 (2 to 3) vs 3 (2 to 3) p=.517	ordinal framework of this
risperidone on the	Screening Checklist (ICDSC):	daily dose of 4 mg.	LOS	6 (5 to 7) vs 6 (5 to 8) p=.056	scale.
incidence of clinical	physician who were trained		Extrapyramidal side effects	2 (3.9%) vs 1 (2%) p=1.0	
delirium in elderly	systematically assessed 4 h	Haloperidol was begun orally at 0.5			it is probable that the
patients who	after extubation and each 8-h	mg q8h and could be escalated to	Adjusted analysis:		study had low power to
underwent on-pump	nursing shift. Define SSD as	10 mg/d if needed. Rescue	Failure to treat SSD with	3.83 (95% CI, 1.63– 8.98; P=.002)	detect a statistically
cardiac surgery.	ICDSC score of 1-3.	medications were started once the	risperidone		significant difference
0, 1		diagnosis of delirium was	Rudolph Risk Score	2.62 (95% CI, 1.51–4.53; P=.001)	between the two groups
Funding source(s):	All patients protocol:	confirmed, and the dosage could	•	/	with regard to ICU,
Support was provided	standardized balanced	be escalated by doubling the dose			hospital length of stay,
solely from	anesthetic technique,	at 24-h intervals, if needed, until			duration of delirium,
institutional and/or	cardiopulmonary bypass, and a	symptoms were controlled or the			highest score on the
departmental sources.	standard protocol was	maximum dosage limit was			ICDSC, or consumption of
• • • • • • • • • •	implemented for sedation,	attained.			antipsychotic medications.
Quality Score = 8	analgesia, and management of				
Risk of Bias: Low	mechanical ventilation after	Rescue medications were			
	surgery (see PDF).	continued for 24h after a score of 0			
	<b>G y (- - - )</b>	was achieved on the ICDSC.			
Conclusion: Using risp	eridone in elderly patients who expe	rienced subsyndromal delirium after or	pump cardiac surgerv was associated	with significantly lower incidence of d	elirium.

### RATING WORKSHEET

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	Based on the intention to treat.
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = Low
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 8

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4-Girard TD, Pandharipande PP, Carson SS, et al. .Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. Crit Care Med. 2010;38(2):428-37.

Study	Bonulation	Intervention Groups		Results	Advarge Effects
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Girard 2010	N = 103 randomized and	n =35 haloperidol every 6	Delirium assessment:	CAM-ICU rated by trained RAs twice	Haloperidol vs
JSA	analyzed	hrs x 14 days	Confusion Assessment	daily based on RASS.	ziprasidone vs
	n = 35 haloperidol	n = 2 discontinued protocol	Method for the ICU (CAM-ICU)	Inter-rater reliability was not discussed.	Placebo
Setting	n = 30 ziprasidone	n = 2 withdrew	RASS		Akathisia:
Multicenter – 6 tertiary	n = 36 placebo	n = 35 analyzed			10 (29%) vs 6 (20%) v
care medical centers		_		Haloperidol vs ziprasidone vs Placebo	7 (19%) (p =0 .60)
		Female, 15 (43%)	Baseline measures	No significant difference between groups	
Study Design	Inclusion	Mean age 51 (35–59)	APACHE II score	26 vs 26 vs 26	Extrapyramidal
Randomized, double-	>18 yrs	,	Brain dysfunction		symptoms
blind, placebo-controlled	ICU patients had abnormal level of	5 mg haloperidol (as a	-Delirium	16 vs 15 vs 17	similar between
trial.	consciousness or were receiving	solution containing 1	-Coma	12 vs 9 vs 14	treatment groups (p
	sedative or analgesic medications	mg/mL)	Haloperidol before enrollment	1 vs 2 vs 4	=0.46).
Randomization method	5	<b>3</b> ,	Ziprasidone before enrollment	0 vs 0 vs 0	,
Computer-generated,	Exclusion	n = 30 ziprasidone every 6	1 '		Comments:
permuted block	N =3194	hrs x 14 days	Primary outcomes	Haloperidol vs ziprasidone vs Placebo	
randomization scheme	1000 neurologic injury	n = 0 discontinued/ withdrew		14.0 (6.0–18.0) vs 15.0 (9.1–18.0) vs	This pilot study was
stratified according to	536 high risk of VT	n = 30 analyzed	Delirium/coma-free days	12.5 (1.2–17.2)	designed primarily to
study center.	344 ventilated >60 hrs				demonstrate the
	190 had no gastric access	Female, 9 (30%)			feasibility of a double-
Study Length/Start-	174 post-suicide attempt	Mean age 54 (47–66)	Secondary outcomes		blind, placebo controll
Stop Dates	108 used neuroleptics	Mean age 54 (47-00)	ventilator-free days hospital	7.8 (0–15.0) vs 12.0 (0–18.6) vs 12.5 (0–	trial of antipsychotics
21-day study period	107 severe dementia	40 mg ziprasidone (as a	ventilator nee days nospital	(p = 0.25), (p = 0.25),	ICU delirium, it was
2/2005 – 7/2007	44 post-liver transplant	solution containing 8		20.0) (p =0.20);	likely significantly
2/2003 - 7/2007	19 pregnant		length of stay	13.8 vs 13.5 vs 15.4 (p =0.68)	underpowered to
Purpose	16 neuroleptic allergy	mg/mL)	length of stay	15.0 vs 15.5 vs 15.4 (p = 0.00)	demonstrate the
To demonstrate the	247 enrolled in other study		21 day martality	4 vs 4 vs 6 (p = 0.81).	potential efficacy for
	210 no informed consent		21-day mortality	4 vs 4 vs 6 (p = 0.01).	
feasibility of a placebo-	2 TO no informed consent	n =36 placebo every 6 hrs			many outcomes
controlled trial of	All notionto protocoli	x 14 days	Average extrapyramidal		including length of stay and survival.
antipsychotics for delirium in the intensive	All patients protocol:	n = 2 discontinued	symptoms score	0 (0–0.2) vs 0 (0–0) vs 0 (0–0) p=0.56	and survival.
	The encoded does of study drug	n = 1 withdrew		Helemeridel := Financidence(OP(Cl), m)	Limitations of the trial
care unit and to test the	The second dose of study drug was administered 12 hrs after if	n = 1 received EoL care	Deily delirium rick	Haloperidol vs ziprasidone (OR (Cl), p)	Limitations of the trial
hypothesis that		n = 36 analyzed	Daily delirium risk	1.2 ( 0.6 –2.2) vs 1.1 ( 0.5–2.2),p= 0.80	include the small
antipsychotics would	QTc interval >500 msec; and then		Cturdu dava dalivaan aad atkan	No Constitue of all frames and	sample size, lack of
improve days alive	q6h.	Female, 14 (39%)	Study drug delivery and other	No significant difference	enforcement by study
without delirium or coma.		Mean age 56 (43–68)	antipsychotics		personnel of a
	Study drug frequency was reduced				standardized sedation
Funding source(s):	to every 8 hrs when patients were	placebo (as a 5-mL solution)			protocol, and the
NIH HL007123, the	two consecutive negative for CAM-				exposure of some
Hartford Geriatrics	ICU.				patients in the
Health Outcomes					ziprasidone and
Research Scholars	Reduced to every 12 hrs when				placebo groups to ope
Award Program, the	patients were delirium/coma-free				label haloperidol.
Vanderbilt Physician	on three consecutive				
Scientist development	assessments, and discontinued				
Program, and GRECC.	when patients were delirium/coma-				
0	free on four consecutive				
Quality Score	assessments.				
6					
	Blood was collected from each				
Risk of Bias:	patient within 48 hrs of study drug				
Unclear	initiation.	1			

Conclusion: A randomized, placebo-controlled trial of antipsychotics for delirium in mechanically ventilated intensive care unit patients is feasible. Treatment with antipsychotics in this limited pilot trial did not improve the number of days alive without delirium or coma, nor did it increase adverse outcomes.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Sponsored by Pfizer, Inc., No ITT, but all randomized were analyzed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = Unclear
8. Sample size ≥50 each study arm (1 point if achieved):	1		
	0		Each group around 35
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the <u>criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

G4 Devlin JW, Roberts RJ, Fong JJ, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. Crit Care Med. 2010;38(2):419-27.

<b>e</b> ( )	<b>_</b>			Results	• • • • ·
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Devlin 2010	N = 258 screened	n = 18 quetiapine 50~200mg	Delirium assessment:	Delirium assessments were completed	More subjects treated with
USA	n = 222 excluded (see below)	q12h 10 days	Intensive Care Delirium	at the subject's bedside formally	quetiapine (6 vs 2)
			Screening Checklist (ICDSC)	educated critical care nurses at	experienced study drug
Setting	N = 36 included in analysis	Men and women (56%)	<b>ö</b> ( , ,	baseline and during every nursing shift.	related adverse events, but
Three academic medical	n = 18 intervention	Mean age = $62.4(14)$		Duration: 10 days	this did not reach statistica
centers ICU	n = 18 placebo			Inter-rater reliability and severity	significance.
		Intervention		assessment not described.	5 = somnolence
Study Design	Dropouts = 10/36 (27.7%)	Study drug or placebo		assessment not described.	1 = hypotension
RCT-double blind,	-1 recovered from delirium	administered:	Baseline characteristics	No significant difference between	
	-2 placebo pts by ICU	Quetiapine was increased	Dasenne characteristics		No episodes of
placebo controlled				groups	
	attending (severe agitation)	every 24 hrs (50 to 100 to 150			extrapyramidal symptoms
Randomization	-3 ICU discharge	to 200 mg every 12 hrs)	Primary outcomes	Quetiapine vs placebo	
method	-4 adverse events	•	time to first resolution of		QTc prolongation was
Assigned in blocks of		Study drug was continued until	delirium (days)	1.0 [0.5–3.0] vs. 4.5 [2.0 –7.0]; p < .001	similar in both groups
four in a 1:1 ratio by	Inclusion	the ICU team discontinued it			
means of a computer-	ICU patients with delirium	because of delirium resolution,	Secondary outcomes (see	Quetiapine vs placebo	Comments
generated random	- ICDSC score ≥4	therapy ≥10 days, or intensive	PDF)		
number table.	Tolerating enteral nutrition	care unit discharge.	Time of study drug	102 (84 -168) vs 186 (108 -228) p= .04	Limitations
	No complicating neurologic	j v	administration (hrs)	· · · · · · · · · · · · · · · · · · ·	-small sample size
Study Length/Start-	condition.	All subjects were allowed to	Time in delirium	36 (12–87) vs 120 (60–195) p=.006	-86% of screened patients
Stop Dates	Informed consent	receive IV haloperidol 1 to 10	-Hours	53 (16–67) vs 69 (58–100) p= .02	excluded
4/2006 – 8/2008	informed consent	mg administered up to every 2	-Percent		-minimum duration of
4/2000 - 0/2000	Exclusion	hrs if nurses observed delirium	Time spent agitated	6 (0–38) vs 36 (11–66) p=.02	study drug not required
Purpose		sx not resolved by study drug		3 (0–22) vs 21 (8–41) p=.03	
	N = 222	sx not resolved by study drug	-Hours	89 vs 56 p=.06	-duration of delirium may
To compare the efficacy	48=Prior antipsychotic use in	Evoluction	-Percent	09 vs 50 p=.00	have been inaccurate
and safety of scheduled	30 d	Evaluation:	Home/rehabilitation center%	0 (0–65)vs 170 (14–1089) p=.02	-discontinuation of study
quetiapine to placebo for	38=receiving enteral nutrition	By trained critical care nurses:	Fentanyl		drug may have been
the treatment of delirium	29=Primary neurological	Sedation-Agitation Scale	-amount per day, ug	0 (0–3)vs 4 (1–9) p=.03	premature
in critically ill patients	condition	(SAS) every 4 to 6 hrs	-total	0 (0–60)vs 70 (17–100)p= .07	-"as needed" haloperidol
requiring as-needed	16=Advanced liver disease	QTc interval at least every 12	- Percent		used for all patients
haloperidol.	12=Alcohol withdrawal	hrs	Study drug	110 (88–191) vs 210 (116–293) p=.01	-greater use of haloperido
	12=Inability to conduct ICDSC	Signs of extrapyramidal	-Daily dose, mg	200 (100–313 )vs 375 (225–400) p=.02	placebo patients could have
Funding source(s):	11=No delirium	symptoms by using the	<ul> <li>Maximum daily dose, mg</li> </ul>		diminished the observed
Supported, in part, by	11=Inability to obtain informed	Simpson-Angus Scale within 1		NOTE: Schedule IV or oral haloperidol	treatment effect of
the Society of Critical	consent	hr then every 12 hrs		and other antipsychotic medications	quetiapine
Care Medicine's Joseph	10=Moribund	-		were not allowed during the study	-did not formally assess
F. Dasta Critical Care	8=Irreversible brain disease	n = 18 placebo 10 days	Delirium assessment:	See above	dementia at baseline
Pharmacy Research	7=Current drug therapy				-short term safety goals
Award and an	w/agents affecting quetiapine	Men and women (56%)	Baseline characteristics	See above	may not have been evenly
unrestricted grant from	concentrations		Dasenne characterístics	See above	distributed (early
AstraZeneca		Mean age = 63.6 (15.3)	Drimony and accordany	Saalahaya	
	6=Current drug therapy with		Primary and secondary	See above	termination of study drug)
Pharmaceuticals.	class la, lc or III	Intervention (see above)	outcomes		
	antiarrhythmics				Future studies should
Quality Score	5=Baseline QTc interval				assess
5	≥500msec				-mortality
	5=Attending physician refusal				-LOS ICU & hospital stay
Risk of Bias:	for enrollment				-post-ICU cognitive
High	7=Other				function
-					-quality of life
					-ability to complete
					activities of daily living.
					-safety for longer duration
					-cost effectiveness

**Conclusion**: Quetiapine added to as-needed haloperidol results in faster delirium resolution, less agitation, and a greater rate of transfer to home or rehabilitation.

### RATING WORKSHEET

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Flow chart listing dropouts (27.7%) did not differentiate between intervention vs placebo
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Possible confounders (see limitations) Drug company sponsorship of study (AstraZeneca) (ITT analysis done but low Nn)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		36 total subjects
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

#### Instructions on rating:

• Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.

- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4-Tahir TA, Eeles E, Karapareddy V, et al. A randomized controlled trial of quetiapine versus placebo in the treatment of delirium. J Psychosom Res. 2010;69(5):485-90.

				sults	1
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Tahir TA 2010	N = 342 screened	n = 21 Quetiapine group	Delirium assessment:	RA conducted screening daily using	Quetiapine vs Placebo
UK	n = 257 no delirium/	n = 5 discontinued	DSM-IV	DSM IV criteria and DRS on medical,	Died within 30 days:
	excluded	-3 deaths	DRS-R-98	surgical and orthopedic wards.	4 vs 3
Setting	n = 115 delirium	-1 adverse events		Patients with delirium (DRS score	Deaths were considered to be
Jniversity Hospital	N = 42 recruited and	-1 doctor stopped med		≥15). Follow up on Days 1, 2, 3, 4, 7,	related to underlying serious
	randomized	n = 16 completed study		and 10.	medical conditions rather than
Study Design	randomizeu	n – To completed study			the study medication
	Inclusion	Man: 6 (28 69/)	Baseline characteristics	No cignificant domographic or	the study medication
RCT (double blind,		Men: 6 (28.6%)	Dasenne characteristics	No significant demographic or	
placebo controlled)	With delirium (DRS-R-	Mean: 84.1 (9.45)		clinical difference between groups	Abnormal involuntary movements
	98>15)				in 10 days:
Randomization		A flexible dosing regime of	Primary outcomes	Quetiapine vs Placebo	4.8% vs 14.3%
nethod		25mg once daily oral	DRS-R-98 Severity	0.827 (0.371, P=.026)	
Computer-generated	Exclusion	quetiapine with dose titration	DRS-R-98 Total	0.55 (0.285, P=.054)	Dropouts (except for death):
andomization codes	N = 257 no delirium	of 25 mg/day to a maximum	DRS-R-98 Cognitive	0.572 (0.443, P=.197)	2 vs 5
	Score <15 on DRS	daily dose of 175 mg in	DRS-R-98 Non-cognitive	0.577 (0.292, P=.048)	
Study Length/Start-	No consent	divided doses.	DRS-R-98 <15 on Day 7	18 (85.7%) vs 17 (80.9%)	One patient was withdrawn from
Stop Dates	Severe physical illness		Maximum dose of guetiapine	40 mg	quetiapine due to complaints of
6/ 2003 to 4/ 2005	Impairment of mental	Dose increased only if DRS-	Maximum dobe of questapine	40 mg	sedation.
5/ 2003 10 4/ 2003	capacity	R-98 and clinical condition	Secondary outcomes		Sedation.
	Severe cognitive deficits		MMSE D1	11.829 (4.080) vs 11.829 (4.080)	Comments
Purpose		did not show any	MINISE DT	11.029 (4.000) VS 11.029 (4.000)	Comments
To determine the	Alcohol withdrawal	improvement			<b>-</b>
efficacy and	Pre-existing psychosis		MMSE D3	16.773 (3.838) vs 16.317 (3.689)	The trial was stopped early at the
acceptability of	Substance dependence	Dose down-titrated if			request of the manufacturer due
quetiapine in the	Inability to comply with the	symptoms improved as	MMSE D10	18.534 (4.757) vs 18.504 (4.739)	to FDA concerns on the use of
treatment of incident	constraints of the trial	indicated by improvement in			antipsychotic medication in the
delirium in general	Contraindications to	DRS-R-98	the Brief Psychiatric Rating Scale	Not reported	elderly.
hospital inpatients	quetiapine		(BPRS)		
with or without minor	• •		Clinical Global Improvement (CGI)	Not reported	A statistically significant
pre-existing cognitive				•	improvement in noncognitive
deficits.	Assessments				items including restlessness,
	Delirium Rating Scale				agitation, thought disorder, and
Funding source(s):	Revised 98 (DRS-R-98)	n = 21 Placebo group	Delirium assessment:	See above	perceptual impairment on the
AstraZeneca UK	MMSE		Demnum assessment.	See above	DRS-R-98 was found on Day 3
	-	n = 7 discontinued	Deservices allowed and the	O a status	
funded RA, trial	Brief Psychiatric Rating	-1 death	Baseline characteristic	See above	with a mean dose of quetiapine
medication and	Scale (BPRS)	-2 withdrew			lower than previously
randomization codes	Clinical Global	-1 noncompliance	Primary outcomes	See above	documented, possibly contributed
	Improvement (CGI)	<ul> <li>1 aspiration risk</li> </ul>			to by the high mean age of 84
Quality Score	Abnormal Involuntary	<ul> <li>1 medication not given</li> </ul>	Secondary outcomes	See above	years.
4	Movements Scale (AIMS)	-cerebrovascular event			
	Medical record case notes	n = 13 completed study			Due to the small sample size, this
Risk of Bias:					should be considered a pilot
High	Follow up	Men: 6 (28.6%)			study.
5.	A follow-up assessment	Mean age: 84.3 (7.16)			······
	was also undertaken on	mean age. 04.0 (7.10)			
	Day 30.				
	Day 50.	Matabing plaashs tablat			
		Matching placebo tablet			

**Conclusion**: Quetiapine has the potential to more quickly reduce the severity of noncognitive aspects of delirium. This study was underpowered for treatment comparisons at specific points in time but nonetheless detected significant differences when analyzing the whole study period. While it is not possible to draw definitive conclusions, further larger studies exploring the use of quetiapine in other delirium populations seem justified. Larger increments in the dose of quetiapine may yield even stronger results.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Discontinued 12/42 (28.6%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	High	Not reported: Brief Psychiatric Rating Scale (BPRS) and Clinical Global Improvement (CGI)
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	AstraZeneca UK sponsored and provided funding No ITT analysis
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		<50 total subjects
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G4- Maneeton B, Maneeton N, Srisurapanont M, Chittawatanarat K. Quetiapine versus haloperidol in the treatment of delirium: a double-blind, randomized, controlled trial. Drug Des Devel Ther. 2013;7(July):657-67.

Study	Bonulation	Intervention Groups		ults	Advaraa Effaata
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Maneeton 2013	N = 408 screened	n = 24 quetiapine 25 mg po.	Delirium assessment:	Frequency: CAM and DRS R 98	extrapyramidal side effects
Thailand	n = 356 excluded	n = 13 completed 7 days of therapy	Confusion Assessment Method	(severity) daily in the evening (5	were assessed by MSAS.
	N = 52 randomized and		(CAM)	pm–10 pm).	
Setting	analyzed	Dropouts = 10	DRS-R-98	Rater: investigator	Quetiapine vs haloperidol
University hospital	n = 24 quetiapine	4 = discharged	D10-11-50	Duration: 7 days	quellapine vs halopendor
University nospital					Completed 7 do thereby
Otrada Datalara	n = 28 haloperidol	2 = adverse events		Inter-rater reliability not	Completed 7 ds therapy
Study Design		2 = early stop medication		described	13 (54.2%) vs 22 (78.6%)
A 7-day prospective,	Inclusion	1 = receiving other antipsychotic			MSAS scores:
double-blind,	18–75 yr	1 = inefficacy	Baseline characteristics	No significant difference	0.3 (0.7) vs 0.3 (1.1) P=.51
randomized controlled	Delirium (DSM-IV-TR, CAM)	1 = died		between groups	Hypersomnia:
trial			Education	> 50% fewer than 6 yrs	10 (41.7) vs 8 (28.6),p=.32
	Exclusion criteria:	Male (%) : 15 (62.5%)			Tremor:
Randomization	Substance-induced delirium	Mean age: 56.6 (12.0)	Primary outcomes:		0 (0) vs 1 (3.6), p=1.00
Using a computer-	Known allergy	<b>o</b> ( )	Duration (days) of delirium	3.3 (2.5) vs 2.9 (2.8), p=.16	Nightmare:
generated	Intolerance to test medicine	Intervention	(,-,-	··· (_··) ·· _·· (_··), p ····	1 (4.2) vs 0 (0), p=.46
randomization system	Pregnancy or breast feeding	The test drugs were continued for	Change in DRS-R-98 severity		Rash:
randomization system	Being on an antipsychotics	24 h after subsidence of SSD (0 on		-22.9 (6.9) vs -21.7 (6.7), p=.59	1 (4.2) vs 1 (3.6), p=1.00
Church a Law white / Chart			score	-22.9 (0.9) vs -21.7 (0.7), p59	
Study Length/Start-	Renal or hepatic failure	the ICDSC) or until ICDSC >3.			Akathisia:
Stop Dates			Secondary outcomes:		0 (0) vs 1 (3.6), p=1.00
7/2009 – 4/2011	Exclusion	Patients who experienced delirium,	DRS-R-98 noncognitive scores	-16.9 (5.5) vs -15.8 (4.7); p=.54	TICS:
	N= 356	the dose of risperidone was			0 (0) vs 1 (3.6), p=1.00
Purpose	153 Alcohol withdrawal delirium	incrementally increased until	DRS-R-98 cognitive scores		
To compare the	80 Received antipsychotics	symptoms were controlled or	response rate	-6.0 (3.2) vs -5.8 (3.6); p =.89	Discharge (n = 4 vs 5)
efficacy and	79 <18 or>75 yrs	attained dose of 4 mg/d.	remission rate	79.2% vs 78.6%,p =.97	Adverse events (2 vs 3)
tolerability between	16 Primary doctors did not allow	5			Early stop med (2 vs 1)
quetiapine and	15 Renal or hepatic failure	Daily assessment:	Time to first remission	2.6 (1.9) vs 1.8 (1.5), p=.14	Receiving other antipsychotics
haloperidol in	5 cannot communicate	Total sleep time per day		HR 1.15 (0.6-2.19), p=.68	(1 vs 1)
	2 Hypoactive delirium	Clinical Global Impression–		11(( 1.15 (0.0-2.15), p=.00	Inefficacy (1 vs 1)
controlling delirious			In any page in total times of allows	$6 = (2, 0) \times (2, 6, 1, (2, 4)) = -74$	
behavior.	2 Inability to obtain consent	Improvement (CGI–I)	Increase in total time of sleep	6.5 (3.0) vs 6.1 (3.4), p =.74	Death (1 vs 1) (not study drug
	2 Seizures	Modified (nine-item) Simpson-			related)
Funding source(s):	2 Disallowance for medication	Angus Scale (MSAS)	CGI–I scores improvement.	-1.1 (1.0) vs -1.2 (1.4), p=.96	<b>•</b> •
Faculty of Medicine,					Comments
Chiang Mai	All patients protocol:	Response and remission rates			
University, Chiang	Orally administered a flexible	(defined as a reduction of the DRS-			In this study, the average dose
Mai, Thailand, grant	dose of quetiapine (25–100	R-98 severity score from baseline			of anti-psychotics in the
number 077/52.	mg/d) or haloperidol (0.5-2.0	for ≥50% and a DRS-R-98 severity			management for delirium was
	mg/d) before bedtime and as	score of 12 or less without relapse.)			relatively low compared with
Quality Score	needed.	, , ,			those applied in previous
6	Adjusted the doses based on	n = 28 haloperidol 0.5 mg po.			studies.
0	the clinical safety, sleepiness,	n = 22 completed 7 days of therapy			
Risk of Bias:	and calmness as measured by	n = 22 completed <i>i</i> days of the apy			As vulnerable subjects, the
		Draw surfa 5			delirious patients aged over 7
Unclear	the DRS-R-98.	Dropouts = 5			
	For all participants, started the	3 = discharge			and severely ill, eg, with renal
	study medication by giving one	1 = adverse events			or hepatic failure, were
	capsule orally at bedtime and	1 = inefficacy			excluded.
	giving one more capsule every	1 = died			
	2–3 hrs for agitation.				
	The maximum dose was four	Male (%): 20 (71.4)			
	capsules per 24 hrs. Other	Mean age: 57.0 (11.9)			
	psychotropic medications,				
	including benzodiazepines, were	Intervention (and shave)			
		Intervention (see above)			
	prohibited.				

**Conclusion**: Low doses of both quetiapine and haloperidol are equally effective and safe for the management of behavioral disturbance in delirious patients.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out 15/52 (29%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = Unclear
	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Total sample: 52
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

# G4-Han CS, Kim YK. A double-blind trial of risperidone and haloperidol for the treatment of delirium. Psychosomatics. 2004;45(4):297-301...

		Results			
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
An 2004 Korea Setting University hospital Study Design A randomized, double- blind trial Randomization nethod A consulting psychiatrist non-investigator) andomly assigned batients ; patients, caretakers and osychiatrist who rated symptoms did not know he drugs prescribed Study Length/Start-Stop Dates ' days Purpose To compare the clinical officacy of risperidone with haloperidol for the reatment of delirium. Studing source(s): Brain Korea 21 Project Quality Score = 5 Risk of Bias: High	N = 28 n = 4 drop out n = 24 complete the study Inclusion With altered mental status Referred to the consulting psychiatry division Exclusion N= not described Dementia Other psychiatric diagnosis Used antipsychotics or benzodiazepines before study Cannot communicate verbally	n = 12 haloperidol for 7 days (flexible dose; initial dose = 0.75 mg) Men/women = 7/5 Mean age: 66.5 (15.9) Intervention A flexible-dose regimen. The initial starting dose of each drug was 0.75 mg (haloperidol) or 0.5 mg (risperidone) twice a day. The dosage was increased depending on the status of delirium during the 7 days. n = 12 risperidone for 7 days (flexible dose; initial dose = 0.5 mg) Men/women = 6/6 Mean age: 65.6 (8.3) Intervention (see above)	Delirium assessment: Confusion Assessment Method Delirium Rating Scale (DRS) Memorial Delirium Assessment Scale (MDAS) Baseline characteristics Medical diagnoses - Fractures -Cerebrovascular accident -Peritonitis -Chronic renal failure -Cancer -Cardiovascular disease - Other Primary outcomes: DRS MDAS response to the drugs average periods before response	Rating of CAM based on DRS at baseline. psychiatrist rated MDAS at the same time daily for 7 days. Inter-rater reliability was not discussed. MDAS for delirium severity Haloperidol vs Risperidone No significant differences 3 vs 4 3 vs 2 1 vs 1 1 vs 2 1 vs 1 2 vs 1 1 vs 1 21.83 (4.43) vs 23.50 (4.19), p=0.35 no significant difference p=0.51 9 vs 5, p=0.11 4.22 (2.48) vs 4.17 (2.14), p=0.95 Delirium Assessment Scale scores of each group decreased significantly during the study period (p<0.05); but there is no significant difference in the efficacy or response rate between haloperidol and risperidone.	None of the 24 subjects showed clinically significant side effects. One patient in the haloperidol group showed mild symptoms of akathisia but was able to tolerate this for the duration of the study.

**Comments:** The author thought differences might exist between Asian and non-Asian populations in the pharmacokinetics of psychotropic agents. Thus, the effective doses might be lower than those given to Caucasian patients.

**Conclusion**: There were no significant differences in efficacy or response rate between haloperidol and risperidone among patients with delirium. Although a larger study might find significant differences it can be cautiously suggested that risperidone is not superior to haloperidol for the acute treatment of delirium.

### RATING WORKSHEET

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out 4/28 (14%) Dropouts not described
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT analysis
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		, , , , , , , , , , , , , , , , , , ,
8. Sample size ≥50 each study arm (1 point if achieved):	0		Only 12 patients each arm
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4- Grover S, Kumar V, Chakrabarti S. Comparative efficacy study of haloperidol, olanzapine and risperidone in delirium. J Psychosom Res. 2011;71(4):277-81.

Study	Population	Intervention Groups	Results		Adverse Effects
Characteristics		intervention Groups	Measure	Outcome	Auverse Effects
Grover 2011	N = 74	n = 20 haloperidol 0.25 to 10 mg	Delirium assessment:	CAM rated by RA based on MSSE	Haloperidol vs risperidone v
ndia	n = 10 drop out		Confusion Assessment	on baseline. Inter-rater reliability	olanzapine
	n= 64 analyzed	Male/Female: 13/7	Method (CAM)	was not discussed.	Total number of subjects who
Setting		Mean age 44.09±16.84	DRS-R98	DRS-R98 for delirium severity.	had side effects
Academic hospital	Inclusion	5			4 vs 2 vs 6
	>18 yrs	Started on haloperidol 0.25 mg			
Study Design	Diagnosis of delirium	twice or thrice daily, gradually	Baseline characteristics	Haloperidol vs risperidone vs	Dropouts
single-blind randomized	based on DRS-R98 and	increased according to the	(no significant difference)	olanzapine	Haloperidol = 6
controlled trial	CAM	necessity, most with 1.5 to 2.5 mg	Education (yrs)	8.09±3.28 vs 8.00±3.95 vs	-2 shifted to ICU
	CAM	daily. 1.25 to 2.5 mg iv and repeat	Education (yrs)	9.35±3.54	-2 comatose
Pondomization mathed	Exclusion	when patient is agitated		9.33±3.34	
Randomization method		when patient is agriated	Duration of delivium prior	41 71 - 22 06 va 64 00 - 60 F1 va	-1 LAMA (left hospital AMA)
computer-generated	N =41		Duration of delirium prior	41.71±22.96 vs 64.00±60.51 vs	Risperidone =1
randomization table	5 Alcohol/benzodiazepine		to assessment (h)	77.20±58.96	-1 LAMA
	withdrawal	n = 21 risperidone 0.25 to 4 mg	DRS-R98 scores (d0)	21.85±4.77 VS 22.56±4.49 VS	Olanzapine = 3
Study Length/Start-Stop	2 Dementia	Male/Female: 14/7		23.80±5.16	-1 shifted to ICU
Dates	7 Terminal illness	Mean age 45.39±19.18	MMSE scores (d0)	6.38±5.02 vs 9.72±6.30 vs	-1 comatose
Not described	3 Comorbid primary	-		6.84±5.33	-1 LAMA
	psychiatric illness	Started on 0.25 to 0.5 mg/day,			
Purpose	5 QTc interval >500 ms	dose increased according to			
To assess the efficacy	3 Parkinson;s disease	requirement, most patients require		Haloperidol vs risperidone vs	
and safety of second-	16 no informed consent	0.5 to 1.5 mg/day.		olanzapine	Comments:
generation antipsychotics		0.5 to 1.5 mg/day.	Primary outcomes	N = 20  vs  21  vs  21	
olanzapine and	All patients protocol:		DRS-R98	10 - 20 03 21 03 21	The sample predominantly
risperidone vs. haloperidol	The doses were titrated	n = 22 clanzanina d 25 to 20 mm	-Day 3	10.14±6.35 vs 11.65±7.24 vs	composed of young adult
in patients of delirium	after daily clinical	n = 23 olanzapine 1.25 to 20 mg	-Day 5		subjects (<65 years)
•	5		Dov 6	11.95±6.82 (P=.43)	subjects (<65 years)
admitted to medical and	assessment; however, if	Male/Female:, 18/5	-Day 6	6.09±7.19 vs 9.17±8.65 vs	This should be the different best of the second
surgical wards.	the patient was agitated,	Mean age 46.50±14.51		8.00±7.27 (P=.424)	This study limited by the smal
	titration was also done				sample size, and did not inclu
Funding source(s):	more than once per day.	Started 1.25 to 5 mg/day, most	DRS-R98 >10 on day 3	12 (57.14%) 14 (60.86%) 12 (60%)	a placebo control arm. In
Institute Research Fund.		patients require 1.25 to 7.5		(P=.967)	addition, the sample only
	Side effects were rated on	mg/day. 2.5 to 5 mg/day if used in	DRS-R98 >10 on day 6	17 (81%) vs 16 (69.56%) vs 14	included those subjects who
Quality Score: 4	the Simpson Angus Scale,	parenteral form.		(70%) (P=.636)	were referred to consultation
-	Abnormal Involuntary	1	Secondary outcomes		liaison psychiatric services, ar
Risk of Bias: High	Movement rating scale		MMSE		the treating physician was not
5	(AIMS) and Udvalg for		-Day 3	17.90±7.37 vs 17.77±7.53 vs	blind to the drug.
	Kliniske Undersogelser		, -	17.57±6.22 (P=.989)	
	(UKU) side effect rating		-Day 6	21.71±7.66 vs 20.77±8.14 vs	
	scale		Dayo	22.31±6.63 (P=.804)	
	source			22.0110.00 (1004)	
	Besides test medications,				
	any medication that can				
	cause delirium and/or was				
	not essential for the care				
	was discontinued. The				
	etiological causes				
	identified for delirium were				
	treated with appropriate				
	measures.				

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	Unclear	Not described
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out: 10/74 (13.5%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCT, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Did not use ITT analysis
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Each group <30
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

# G4-Kim SW, Yoo JA, Lee SY, et al. Risperidone versus olanzapine for the treatment of delirium. Hum Psychopharmacol. 2010;25(4):298-302.

			Re		
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Kim 2010	N = 32	n = 17 risperidone 7 days	Delirium assessment:	Frequency: Evaluated at the	Drop outs:
Korea	n = 17 risperidone	n = 12 (70.6%) completed study	Delirium Rating Scale-	same time every day.	n = 10 discharge from hospital
	n = 15 olanzapine		Revised-98 (DRS-R-98)	Rater: Blinded investigators	n = 2 withdrawal of consent
Setting		Men and women: (53%)	, , , , , , , , , , , , , , , , , , ,	Duration: 7 days	
University hospital	Inclusion	Mean age: 66.7 (12.1)		Inter-rater reliability not discussed	Risperidone vs olanzapine
	Delirium patients (by DSM-IV)				N = 13
Study Design		Intervention			Tremor and bradykinesia
Randomized,	Exclusion	The mean starting dose was 0.6			n = 2 (11.8%) vs 1 (6.7%)
comparative clinical	N= not described	+-0.2 mg/day risperidone (range,	Baseline characteristics	No significant difference	
rial	Dementia	0.25-1  mg/day (spendone (range, 0.25-1 mg/day)		between groups in demographic	Exacerbation of daytime
	Serious hepatic problems	0.25-1 llig/day)		or clinical characteristics	somnolence or increased
Randomization	Bone marrow suppression	The mean does at last cheen ation		or clinical characteristics	duration of sleep
method	Taken antipsychotics	The mean dose at last observation	Primary outcomes:	Risperidone vs Olanzapine	n = 5 (29.4%) vs 5 (33.3%),
Not described in	Undergoing intubation	was 0.9+-0.6 mg/day risperidone	DRS-R-98 score	25.8 (5.2) vs 23.5 (5.1) p=.217	p=1.000)
	Cannot communicate verbally	(range, 0.25–2 mg/day)	DR3-R-90 SCOLE	20.0 (0.2) vs 20.0 (0.1) p=.217	p=1.000)
detail; recruitment	Cannot communicate verbaily				
rom patients who met					All extrapyramidal symptoms
nclusion criteria	All patients protocol:		Secondary outcomes:		were tolerable and mild to
	All outcome measures were		Response rate		moderate.
Study Length/Start-	evaluated at the same time	n = 15 olanzapine 7 days	-Total	64.7% vs 73.3%; p=.712	
Stop Dates	every day for 7 days.	n = 8 (53.3%) completed study)	Age ≥ 70 yrs	33.3% vs 70%; p=.024	Comments:
12/2007 – 11/2010			Age <70 yrs	100% vs 80%	These doses were relatively lo
_	Blinded investigators assessed	Men and women (60%)			compared with those in
Purpose	daily, without recognizing the	Mean age: 68.3 (10.7)	Median time to response (d)	5 vs 3; p=.298	previous studies of risperidone
To compare the	study medication. The initial				and olanzapine.
effectiveness of	starting dose was based on age,	Intervention			
risperidone and	medical condition, and delirium	The mean starting dose was 1.8+-			A more rapid and higher
olanzapine in the	severity, and the dosage was	0.6 mg/day olanzapine (1.25– 2.5			increase in the drug dose mig
treatment of delirium.	increased over 7 days,	mg/day).			have increased the efficacy of
	depending on the delirium				the study medications in the
Funding source(s):	status.	The mean dose at last observation			treatment of delirium, although
Grant (CRI08019-1)		was and 2.4+-1.7 mg/day			the response rates in our stud
of the Chonnam	Strict prohibition of rescue	olanzapine (1.25–7.5 mg/day).			were not much different from
National University	medication in patients with poor				those in previous studies.
Hospital Research	physical status would have				
nstitute of Clinical	produced ethical conflicts;				The limitation s of this study a
Medicine.	therefore, rescue IM injection of				small sample size and
	haloperidol or benzodiazepine				factors such as the use of
Quality Score	was permitted and recorded as				rescue injections that cannot b
3	an outcome variable.				strictly controlled.
Risk of Bias:					
High					
		1			

Conclusion: Risperidone and olanzapine were equally effective in reducing delirium symptoms. The response to risperidone was poorer in the older age group.

# RATING WORKSHEET

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Not described
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Reported: "rater blind study design: "psychiatrists randomly assigned patients". No other blinding described
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out 12/32 (37.5%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs, lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	"main analyses performed on modified ITT basis" but Very high dropout (37.6%)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Total N= 32
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G4-Skrobik YK, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. Intensive Care Med. 2004;30(3):444-9.

				Results	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Skrobik YK 2004	N = 1009 admitted to ICU	n = 45 haloperidol group	Delirium assessment:	Daily rating ICU-DSC by a clinician or	Haloperidol vs Olanzapine
Canada	N = 214 delirium dx		ICU Delirium Screening	research nurse; physician	
	n = 111 excluded (see below)	Men and women: 31%	Checklist (ICU-DSC)	determined if DSM IV criteria met. DI	extrapyramidal symptom testing
Setting	N = 103 eligible for randomization	Mean age 63.26 (11.66)	Delirium index (DI)	for delirium severity daily. Overall	6 rated low scores vs 0
Tertiary care	N = 80 provided informed consent		DSM IV	agreement regarding DI scores CCI =	
university affiliated	n = 7 dropouts	Haloperidol was initiated at		0.96.	No patient in either group received
critical care unit	3 = treating physician withdrew	2.5–5 mg every 8 h			prophylactic or therapeutic
	patient		Baseline characteristics	Significant difference between	antiparkinsonian therapy.
Study Design	2 = status changed to "no active	Daily dose 6.5 mg (range		groups	
Prospective	treatment)	1–	Age	63.26 (11.66) vs 67.50 (6.04) p = .05	There were no adverse effects
randomized trial	1 = drug interaction suspected	28 mg)			(specific or otherwise) attributable
	1 = data was lost		Outcomes	All patients	to olanzapine.
Randomization		Protocol for all patients:	daily DI scores	7.08 (day 1) to 5.05 (day 5) NS	
method	N = 73 in analysis analysis	The intensivist prescribed	Time effect	P = .02	Comments
Randomized based		the antipsychotic orally or	Group effect and		
on even vs odd date	Inclusion	via enteral tube within 2 h	interaction effect	NS (see Fig 1)	Both olanzapine and haloperidol
	Age 18–75 yrs	of the diagnosis of			were effective in reducing delirium
Study Length/Start-	Admitted to ICU >24 hrs	delirium.	Dose of benzodiazepines	NS (lorazepam equivalents)	symptoms.
Stop Dates	Delirium dx		Time effect	P = .02	
7/2000 - 9/2001	Informed consent	Patients over 60 years	Group and interaction		The clinical course in both
		received a lower initial	effect	NS (See Fig 2)	treatment arms was unmarred by
Purpose	Exclusion	dosage (haloperidol 0.5-1			severe agitation.
To compare the	N = 111 (exclusions	mg, or olanzapine 2.5 mg).	Dose of rescue		-
safety and estimate	were due primarily to	Subsequent titration was	haloperidol, opiates or		Intravenous rescue haloperidol,
the response profile of	gastrointestinal dysfunction	based on clinical judgment.	sedatives (other than BZD)	NS (no figure or specific data)	used in the first 24 h in both
olanzapine, a second-	preventing oral/enteral				groups, may have contaminated
generation	administration)	n =28 olanzapine group	Delirium assessment:	See above	the early DI evaluation between
antipsychotic, to	Pregnant				the groups.
haloperidol in the	Antipsychotics within 10 days before	Men and women: (21%)	Baseline characteristics	See above	
treatment of delirium	admission	Mean age : 67.50 (6.04)			Given the reported half life of
in the critical care	Test drug were contraindicated	<b>o</b> ( , ,	Primary outcomes	See above	intravenous haloperidol, however,
setting.	Parkinson's disease	Olanzapine was begun at	-		and the small number of patients
0	Oropharyngeal dysfunction	5 mg daily	Secondary outcomes	See above	who required it beyond the first
Funding source(s):	Prolonged QT interval	0,	2		day, it is unlikely the overall
Grant from the	Hepatic or renal dysfunction	4.54 mg for the olanzapine			beneficial evolution of the
Zyprexa fund, Eli-Lilly,	Gastrointestinal dysfunction	group			olanzapine group over time is
North America	precluding oral/enteral drug	(range 2.5–13.5 mg)			attributable to the rescue
	administration				haloperidol received on the first
Quality Score	Neurological condition preventing				day.
1	neuropsychiatric evaluation				-
		Protocol for all patients:			There was uneven distribution
Risk of Bias:	Assessments	See above			between the two treatment
High	Acute Physiology				groups. The odd/even day
	and Chronic Health Evaluation				randomization, chosen for
	(APACHE II)				convenience, was not corrected
	Daily worst Ramsay score				for the slightly more frequent
	Extrapyramidal signs assessed with				occurrence of odd days on which
	Ross-Chouinard and				patients were randomized to
	Angus-Simpson scales by a				receive haloperidol in this study.
	physician				
		•	•	•	

Conclusion: Olanzapine is a safe alternative to haloperidol in delirious critical care patients, and may be of particular interest in patients in whom haloperidol is contraindicated.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Not a valid randomization procedure
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	randomization on an even/odd day; no further description
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Not described
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	No detail (n) of exclusions
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	Unclear	Reporting of outcomes provided limited specific data
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: Lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Drug company sponsorship of study No ITT Baseline imbalance for age
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING =High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		>50 in each group
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 1

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G4-Yoon HJ, Park KM, Choi WJ, et al. Efficacy and safety of haloperidol versus atypical antipsychotic medications in the treatment of delirium. BMC Psychiatry. 2013;13:240.

Study Characteristics	Population	Study Groups	Measure	Outcome	Adverse Effects Comments
Yoon HJ 2013 Korea Setting Tertiary level university hospital Study Design Prospective, comparative clinical observational study Selection method Patients presenting with mental status change referred to consultation	N = 146 screened n = 130 met delirium dx criteria n = 33 with delirium excluded N = 80 included* N = 53 completed trial Dropouts -18 = discharge -6 = transfer to ICU -3 = consent withdrawn Inclusion Age >50 Met DSM-IV-TR criteria for delirium dx Informed consent	n = 23 haloperidol group n = 9 dropouts -5 = discharged -2 = transferred to ICU -2 = consent withdrawn Men and women (47.8%) Mean age 74.0 ± 9.9 Flexible dosing regimen: haloperidol: 0.5-10 mg,	Delirium assessment:         DSM-IV-TR         Korean version of the Delirium         Rating Scale-Revised-98         (DRS-K)         Baseline characteristics         Primary outcomes         Efficacy         Mean DRS-K baseline vs Day 6	All the subjects were evaluated at baseline and on the 2nd, 4th, and 6th days at the same time of day (PM 7:00– 9:00). DRS-K for delirium severity. There was no significant difference between groups for demographic or clinical variables The within group effect was significant in all groups A serial decrease in the mean DRS-K severity score and increase in mean K- MMSE score was observed in all groups 17.4 (6.7) vs 7.7 (5.4)	Comments Dropouts: No significant difference ir dropouts between study groups Safety: No significant difference between groups Sedation = 4 (17.3%) Dystonia = 0 (0%) Rigidity = 2 (8.7%) Bradykinesia = 1 (4.3%) Tremor = 3 (13.0%) Akathisia = 1 (4.3%) Total = 5 (21.7%)
psychiatric liaison service Study Length/Start- Stop Dates 6-days Purpose To compare the efficacy and safety of haloperidol versus three atypical antipsychotic	Exclusion N = 33 8 = Dementia or comorbid psychiatric disorder 7 = Terminal illness 3 = Hx prolonged QTc interval 2 = Hearing loss 1 = Neuroleptic malignant syndrome 1 = Use of antipsychotic medication before referral	n = 21 risperidone group n = 7 dropouts -5 = discharged -2 = transferred to ICU Men and women (61.9%) Mean age 70.1 ± 9.5 Flexible dosing regimen risperidone: 0.25-4 mg	Mean K-MMSE baseline vs Day 6 Delirium assessment Primary outcomes Efficacy Mean DRS-K baseline vs Day 6 Mean K-MMSE baseline vs Day 6	13.7 (6.5) vs 22.4 (4.4)         See above         18.9 (5.2) vs 8.3 (7.1)         15.0 (5.8) vs 22.4 (5.0)	Sedation = 3 (14.2%) Dystonia = 0 (0%) Rigidity = 1 (4.7%) Bradykinesia = 1 (4.7%) Tremor = 2 (9.5%) Akathisia = 0 (0%) Total = 4 (19.0%)
antipsychotic medications (risperidone, olanzapine, and quetiapine) for the treatment of delirium with consideration of patient age. Funding source(s): Not disclosed	Assessment Delirium Etiology Checklist (DEC) K-MMSE (Korean version) Udvalg Kliniske Undersogelser (UKU) for side effects	n = 18 olanzapine group n = 5 dropouts -4 = discharged -1 = transfer to ICU Men and women (55.6%) Mean age 69.5 ± 15.9 Flexible dosing regimen olanzapine: 1–20 mg	Delirium assessment Primary outcomes Efficacy Mean DRS-K baseline vs Day 6 Mean K-MMSE baseline vs Day 6	See above 17.5 (5.7) vs 8.1 (5.5) 16.2 (5.4) vs 23.1 (5.3) The response rate to olanzapine was poor in subjects > 75 yrs old compared to those <75 yrs old	Sedation = 2 (22.2%) Dystonia = 0 (0%) Rigidity = 1 (5.5%) Bradykinesia = 0 (0%) Tremor = 1 (5.5%) Akathisia = 0 (0%) Total = 4 (22.2%)
Quality Score 2 Risk of Bias: High	*NOTE: No CONSORT chart and numbers reported do not reduce to 80.	n = 18 quetiapine group n = 6 dropouts -4 = discharged -1 = transfer to ICU -1 = consent withdrawn Men and women (55.6%) Mean age 73.3 ± 10.7 Flexible dosing regimen quetiapine: 25–200 mg	Delirium assessment Primary outcomes Efficacy Mean DRS-K baseline vs Day 6 Mean K-MMSE baseline vs Day 6	See above 17.5 (6.4) vs 6.5 (4.0) 15.7 (6.3) vs 23.4 (3.2)	Sedation = 2 (11.1%) Dystonia = 0 (0%) Rigidity = 1 (5.5%) Bradykinesia = 0 (0%) Tremor = 1 (5.5%) Akathisia = 0 (0%) Total = 2 (11.1%)
	or of age needs to be consider			ce between age groups and response rate for All of the atypical antipsychotics studied wer	

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Low	No significant differences between groups in demographic or clinical variables reported
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out = 27/80 (34%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Possible confounders inadequately controlled Funding source not described.
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		(assuming Korean version is validated)
8. Sample size ≥50 each study arm (1 point if achieved):	0		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 2

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G4-Breitbart W, Marotta R, Platt MM, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. Am J Psychiatry. 1996;153(2):231-7.

Study	Population	Intervention Groups	Maasuus	Results	Adverse Effects
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Breitbart W 1996	N = 419 approached for	n = 11 haloperidol	Delirium assessment:	Trained research staff monitored study patients	No significant difference
USA	participation	•	DSM III R	daily for signs of delirium. Medical and nursing	-medical complications
	N = 244 informed consent	Treatment group-specific	Delirium Rating Scale	staff also trained. If delirium was suspected the	p<0.32
Setting		demographics not	MMSE	study coordinator and study psychiatrist	-severity of complications
_arge metropolitan	N = 30 developed delirium	described	initio E	performed a full assessment	p<0.61
Cancer Center		deserbed		Each study drug treatment protocol initiated	p<0.01
Cancel Center	Men and women (23%)	Treatment protocol		(blinded); patients evaluated hourly with DRS,	Deaths (within 8 days of
Study Design		established for each study		MMSE and ESRS	
	Mean age 39.2 (8.8) (23-56)	-		WIWISE AND ESRS	protocol initiation)
RCT (double blind)	Inclusion	drug.	Deceline characteristics	No significant differences between the streamt	n = 2 haloperidol
	Inclusion	Dose level mg (1-9) for oral	Baseline characteristics	No significant difference between treatment	n = 2 chlorpromazine
Randomization	AIDS-related medical problems	and intramuscular		groups	n = 1 lorazepam
method	Medically stable	administration	<b>_</b>		
Hospital pharmacy	Informed consent (to delirium		Primary outcomes	Haloperidol vs chlorpromazine vs lorazepam	Deaths within 1 week afte
conducted	protocol if delirium developed)	Table 1, p 233 in PDF	Mean dose first 24 h (mg)	2.8 (2.4) vs50 (23.1) vs 3.0 (3,.6)	completing the protocol
randomization; also	Delirium present during study		Average maintenance dose	1.4 (1.2) vs 36.0 (18.4) vs 4.6 (4.7)	n = 3 chlorpromazine
identified study drug if	period				n = 1 lorazepam
significant adverse			Average DRS baseline	20.45 (3.45) vs 20.62 (3.88) vs 18.33 (2.58)	
effects occurred	Exclusion		Average DRS day 2	12.45 (5.87) vs 12.08 (6.50) vs 17.33 (4,18)	Extrapyramidal side
	N = 175 (no specific data)		Average DRS end of tx	11.64 (6.10) vs 11.85 (6.74) vs 17.00 (4.98)	effects = none
Study Length/Start-	Hypersensitivity to neuroleptics		Main effect for time	F = 10.09, df=2,27, p<0.001	-no effect for time,
Stop Dates	Hypersensitivity to			Main effect for drug NS (p<0.44)	p<0.81
28 weeks	benzodiazepines		Significant decrease in DRS	·······	-drug by time interaction
20 1100110	Presence of neuroleptic		Baseline to day 2	F = 27.50, df=1, 27, p<0.001	= trend, p<0.07
Purpose	malignant syndrome		No significant difference in	·	-increase in lorazepam
To determine the	Concurrent treatment with		DRS day 2 to end of tx	P<0.43 vs p<0.81 vs p<0.81	group
safest and most	neuroleptic drugs			1 40.40 10 p 40.01 10 p 40.01	group
effective	Seizure disorder	n = 13 chlorpromazine	Delirium assessment:	See above	Comments
pharmacotherapies	Current systemic chemo-	n – 13 chiorpromazine	Demnum assessment.	See above	Comments
for the management	therapy	Treatment restand			This study confirmed the
5		Treatment protocol – see	Primary outcomes		
of the mental	Withdrawal syndrome	above	Significant decrease in DRS		clinical efficacy of
symptoms and	Anticholinergic delirium	Table 1, p 233 in PDF	Baseline to day 2	F=37.02, df=1, 27, p<0.001	neuroleptic drugs in the
behavioral	Current or past dx			MMSE improved only for chlorpromazine group	amelioration of delirium
disturbances	-schizophrenia		MMSE baseline to day 2	F=13.99, df=1,27, p<0.001	symptoms in AIDS
associated with	-schizoaffective disorder		MMSE baseline to end of tx	F=4.68, df=1,27, p<0.04	patients.
delirium in AIDs	-bipolar disorder				
patients.	Participation would				In addition, lorazepam
	compromise obtaining needed	n = 6 lorazepam	Delirium assessment	See above	alone is not effective in the
Funding source(s):	medical treatment				treatment of delirium in
Not described	Delirium associated with	Treatment protocol – see	Primary outcomes		AIDS patients,
	terminal event	above	No significant decrease in		
Quality Score	Lacked capacity for informed	Table 1, p 233 in PDF	DRS Baseline to day 2	F=0.23, df=1,27, p<0.63	The doses of neuroleptics
3	consent		-		required to manage
			Treatment-limiting side	All 6 patients developed side effects	delirium in AIDS patients
Risk of Bias:	Assessments		effects	-increased confusion	may be considerably lower
Unclear	Delirium Rating Scale (DRS)			-oversedation	than many reported in
	DSM III R			-disinhibition	clinical standards.
	MMSE (also used to guide			-ataxia	
	ratings on delirium severity)			Lorazepam treatment discontinued	There may be disease
	Extrapyramidal Symptom				specific mechanisms that
	Rating Scale (ESRS)			Subsequent patients randomized to haloperidol	explain why patients with
	Side Effects and Symptoms			or chlorpromazine	AIDS required low doses.
	Observation				
	Checklist				
	Montol Status Drafile			fects by using low-dose neuroleptics (haloperidol or	

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	Unclear	Baseline date not reported except for age and gender of 30 patients with delirium
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not clear whether outcome assessors were blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Total patients approached and number consented, but no specific data on exclusions
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	All patients analyzed, but ITT protocol not performed Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:
   Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:

   o
   Low risk of bias:
   Low risk of bias:

   o
   Unclear risk of bias:
   High or unclear risk of bias on 1 or more of 6 domains

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  - High risk of bias: High risk of bias on 2 or more of 6 domains

**G1**-Sieber FE, Zakriya KJ, Gottschlack A, et. al., Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair, Mayo Clinic Proc. 2010; 85(1):18-26.

Study Donulation		Intervention Crows	Res		
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects Comments
Sieber F 2010	N= 457 hip fracture patients	n = 57 Deep sedation	Delirium assessment:	Trained research nurse performed	Adverse Effects
JSA	screened	group	CAM	daily CAM from 2 <sup>nd</sup> day post-op.	None reported
	n = 54 not eligible	n = 4 converted to		until discharge at approx. 10am	
Setting	n = 289 not randomized	general anesthesia		<b>o</b> 11	
Iohns Hopkins Bayview		5		Deep (57) v Light (57) Sedation	
Aedical Center	N= 114 Randomized	Men and women (75.4%)			Comments:
	n = 57 Deep sedation	Mean age = $81.8\pm6.7$	Baseline characteristics	No significant differences	One limitation of the currer
Study Design	n= 57 Light sedation	MMSE score, mean	Bucchine characteristics	No significant anterences	study is the exclusion of
RCT – parallel groups	n = 0 withdrew	24.5±5.3	Intra-operative Data	Significant differences	patients with MMSE score
(C) – parallel groups		Pre-op MMSE <24 = 21	Duration of Surgery (min)	93 (44) v 79 (33) , p=0.05	of less than 15, restricting
Randomization method	Inclusion	(37)		10.2 (5.6) v 2.5 (2.7), p<.001	the generalizability of the
	-Aqe ≥65 vrs	(37) Depression = 14 (25)	Propofol dose (mg/kg)		
Patients were randomized			Receiving midazolam	3(5) v 11(19), p=.04	results to patients with at
o receive deep or light	-Hip Fracture repair surgery	Benzodiazepine use = $2$	Midazolam dose	1.26 (6.36) v 5.53 (12.42), p=.02	most moderate dementia.
sedation using a	-Spinal anesthesia	(4) Antidepressant use	Average BIS, mean (SD)		
andomized block design	-Propofol sedation	=10 (18)	Range 0-100	49.9 (13.5) v 85.7 (11.3), p <.001	Dementia assessment in the
with random length blocks.	-Informed consent	Opioid use = $4(7)$	Average BIS <50, mean (SD)	48 (34) v 4 (18), p <.001	study might have been mo
Randomization					reliable using a clinical
ncorporated a stratification	Exclusion		Primary outcomes		consensus, rather than
cheme for age (>80 years	-N=170	Intervention	Postoperative delirium	23 (40) v 11 (19), p=.02	primary care physician
or 65-80 years) and	<ul> <li>n=10, Refusal of spinal anes</li> </ul>	Bispectral index (BIS)			diagnosis and the MMSE.
ognitive impairment	<ul> <li>n=4, Language barriers</li> </ul>	monitoring targeted to	Significant secondary		_
MMSE score, 24-30 or 15-	- n=42, Pre-op cognitive	approximately 50	outcomes		All data analyzed on ITT
23). Blinding of all study	impairment (MMSE score <15)		Duration of delirium, (all patients)		basis
eam members except	- n=37, Pre-op delirium (+CAM		mean (SD) d	1.4 (4.0 ) v 0.5 (1.5), p=.01	
attending anesthesiologist	score)		Delirium in patients with:		
ggg	- n=61, pre-op dementia and		pre-op MMSE(score ≥20)	14(44) v 5(14), p=.01	
Study Length/Start-Stop	delirium		pre-op MMSE(score ≥24)	$11(39) \times 3(11), p=.03$	
Dates	-n=16. Contraindications to			(i), p	
4/2/2005-10/30/2008	spinal anesthesia	n = 57 light sedation	Delirium assessment:	See above	-
12/2003-10/30/2000	e.g.: Aortic stenosis	group	Baseline characteristic	See above	
Purpose	Coagulopathy	n = 6 converted to	Primary outcomes	See above	
To determine whether	0,1,9				
	Anticoagulants use	general anesthesia	Secondary outcomes	See above	
imiting intraoperative	Spinal cord disease	Men and women (70.1%)			
sedation depth during	- Prior hip surgery	Mean age = $81.2\pm7.6$	Significant Predictors of Post-	OR (CI), p	
pinal anesthesia for hip	- Mental barriers	MMSE score, mean =	operative Delirium (univariate		
racture repair in elderly	- Severe congestive heart failure	24.8±4.6	analysis)		
patients can decrease the	- Severe COPD	Pre-op MMSE <24 = 19	Deep vs light sedation	2.83 (1.20-6.62), p = .01	
prevalence of		(33)	Average BIS	0.97 (0.954-0.995), p=.01	
oostoperative delirium.	Protocols (all patients)	Depression = $11(19)$	Duration BIS <50	1.001 (1.00-1.023), p=.05	
	Pre-op screening	Benzodiazepine = 3 (5)	Preoperative dementia	3.56 (1.52-8.32), p=.003	
Funding source(s):	MMSE	Antidepressant use = 9	Preop MMSE score	0.86 (0.78-0.95), p=.001	
Grant	CAM	(16)	Preoperative ADL	0.72 (0.54-0.98), p=.02	
K08AG029157/AG/NIA NIH		Opioid use = $2(4)$	Units of packed		
HHS	Standardized :	-	erythrocytes transfused	1.58 (1.12-2.22), p=.007	
	-Intra-op monitoring	Intervention	≥1 Postop complications	2.48 (1,.07-5.75), p=.03	
Quality Score	-Anesthesia administration	BIS monitoring target to	No. of post-op complications	1.50 (1.08 -2.09), p=.02	
3	(≤2mg midazolam, 11.25 mg	approximately 80 (or	Admission to ICU without prior		
-	0.75% bupivacaine)	higher)	delirium	8.19 (1.44-46.4), p=.02	
Risk of Bias:	-Post-op analgesics	ingrici)	Length of ICU stay	1.28 (1,.02-1.59), p=.02	
				1.2011.02-1.001.002	

**Conclusion**: The use of light propofol sedation decreased the prevalence of postoperative delirium by 50% compared with deep sedation. Limiting depth of sedation during spinal anesthesia is a simple, safe, and cost-effective intervention for preventing postoperative delirium in elderly patients that could be widely and readily adopted.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Low
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		САМ
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 8

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

**G1-** Santarpino G, Fasol R, Sirch J, et. al. Impact of bispectral index monitoring on postoperative delirium in patients undergoing aortic surgery, HSR Proc Intensive Care Cardiovasc Anesth. 2011; 3(1): 47-58.

Cturder.	Population	Maariina	Creation	Creation II	Results	Crown IV	Creating V	
Study Characteristics	Population	Measure	Group I n=52	Group II n=125	Group III n= 68	Group IV n=33	Group V n=14	Significant difference between groups
			BIS Reduc ≤15%	<b>BIS Reduc</b> 15-20%	BIS Reduc 20-25%	<b>BIS Reduc</b> 25-30%	BIS Reduc >30%	groups
Santarpino G	N = 292	Delirium assessment:						Preoperative (Baseline)
2011	n = 53 BIS reduction ≤15%	DSM-IV						Significant differences for
Deutschland	n = 125 BIS reduc 15-20%	Differential dx performed by						dissections (v elective)
Dettine a	n = 68 BIS reduc 20-25%	anesthesia staff in the ICU.						- Age (older p<0.001)
Setting	n = 33 BIS reduc 25-30% n = 14 BIS reduc >30%							- Hypertension (more p<0.001)
Inpatients (Clinical and hospital	II = 14 BIS reduc > 30%	Baseline characteristics						- Hypercholesterolemia (more p 0.017)
records)	Inclusion	Age (years)	59.7±15	60.0±14.3	60.2±11.9	53.6±11.2	58.7±10.9	- Intubation times (p<0.001)
00003)	- Age ≥18	EuroSCORE	10.3±3.2	10.2±3.6	9.9±2.8	10.7±3.5	10.1±3.2	- CPB times ( p<0.001)
Study Design	- Aortic surgery	Height (cm)	172.1±9.2	172.7±9.5	171.9±10.2	177.8±10.8	174.9±8.4	- Cross-clamping times (p <0.00 <sup>2</sup>
Observational -	- Replacement of	Weight(kg)	80.4±13.9	81.4±16.7	84.6±25.2	84.6±14.5	81.4±14.4	- Length of ICU stay( p <0.001)
Retrospective	ascending aorta combined	NYHA class	1.2±1.4	1.3±1.5	1.0±1.3	0.7±1.3	1.1±1.3	- Body temperature (p < 0.001)
analysis	with	LVEF (%)	63.5±11.7	59.2±12.8	60.7±10.2	58.4±10.9	61.3±8	Cumulative difference in:
	-aortic arch,	Procedure time (min)	272±126	285.7±115.9	268.0±117.0	287±113.2	331±117.7	-Delirium, p<0.001
Selection	<ul> <li>valve replacement or</li> </ul>	CPB time (min)	165.2±94.1	165.8±76.2	162.2±83.2	171.6±70.1	205.4±89.	-Neurological events, p<0.001
method	-coronary artery bypass	Cross-clamping time (min)	95.7±50.5	88.4±36.8	93.4±43.4	101.5±44.6	7	-Length of ICU stay, p=0.003
Consecutive		Minimum temp (C)	28.7±6.0	28.5±5.4	29.1±5.6	26.8±6.5	108.2±50	-Intubation time, p=0.001
patients fitting	Exclusions						26.5±6.6	Post hoc analysis:
nclusion criteria	Clinical instrumental	Type of surgery	<u> </u>	0(4.00()	4(00()	1	<u> </u>	- Only Group V showed a longer
N	findings showing postop	Ascending aorta + CABG	0	2(1.6%)	1(3%)	(3%)	0	ICU stay compared to
Study _ength/Start-	-low cardiac output -acute renal or liver failure	Ascending aorta + AVR Ascending aorta – AVR	32(61%) 16(31%)	72(57.6%) 42(33.6%)	22(66.7%) 8(24.2%)	22(66.7%) 8(24.2%)	6(43%) 4(29%)	-Group I (p=0.002), -Group II (p=0.005)
Stop Dates	Not entered in database as	with arch	4(7.7%)	9(7.2%)	2(6.1%)	2(6.1%)	4(29%)	-Group III (p=0.005)
12/2006-12/2009	associated with postop	with arch	4(7.770)	9(1.270)	2(0.170)	2(0.170)	4(2970)	- Group V also showed a longer
12/2000-12/2005	delirium and not analyzed	Primary outcomes						intubation time compared to
Purpose	dominant and not analyzou	Incidence of delirium (N = $53$ )	3(5.8%)	5(4%)	5(7.4%)	30(90.9%)	10(71%)	-Group I (p=0.008)
To evaluate the	Protocol	Delirium requiring therapy	2(3.8%)	4(3.2%	1(1.5%)	15(45.5%)	9(64%)	-Group II (p=0.002).
ole of Bispectral	Standardized:	1 0 19	· · /	,	<b>、</b>	, ,	× ,	- Length of ICU stay
index (BIS) in	-Anesthetic technique							-Group I vs V (p=0.013)
ostoperative	- Cardiopulmonary	Neurological complications (N						- Group II vs V (p=0.023)
neurological	bypass (CPB)	= 29)						- Intubation time
outcome of	-Surgical technique	TIA	0	0	0	0	1(7.1%)	-Group II vs V (p=0.01).
patients	-Post-op care	RIND	0	2(1.6%)	1(1.5%)	0	0	- Incidence of neurological
undergoing aortic		Stroke	3(5.8%)	4(3.2%)	1(1.5%)	6(18.2%)	11(79%)	events
surgery, with	BIS Reduction	Conservations and a man						-higher in Group V (p<0.001)
special reference to motor function	Calculation Baseline BIS value and the	Secondary outcomes	3(5.8%)	9(7.2%)	4(5.9%)	1(3%)	2(14%)	- Incidence of delirium -Group IV (p<0.001)
and delirium.	minimum BIS value	Mortality Intubation time	3(5.8%) 73.3±112	9(7.2%) 105.2±177.8	4(5.9%) 106.6±209.4	133.5±169	2(14%) 228.2±211	Aortic dissections vs elective
	recorded during surgery	ICU length of stay	5.4±6.6	7.3±8.6	6.7±6.5	8.7±8.3	.3	surgery
unding	was determined (baseline	100 length of stay	0.410.0	7.510.0	0.710.5	0.710.0	.0 13.5±10.3	Aortic dissection
source(s):	value-minimum						10.0110.0	-All deaths (n=19, p<0.001).
Not disclosed	value/baseline value x							- Higher incidence of post-op
	100).							neurological events (p=0.01)
Quality Score	Time interval was							- Higher incidence of delirium
3	arbitrarily set to >15 min to							(p=0.007)
	minimize the rate of false							-Higher incidence of delirium
Risk of Bias:	positives							requiring therapy (p=0.03).
High								
<b></b>			<u></u>					
onclusion: Intraop	perative cerebral monitoring wit	In BIS can predict postoperative de	elirium when a E	SIS reduction of	25-30% is observ	ved. Several co	ntounding fac	tors likely affected the reported BIS
	indings are confirmed by addition of the studies are warranted to cl	ional research, they would translate	e to improved q	uality of care, E	xpianations of th	ese findings are	speculative w	vith regard to the underlying g

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jaded scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	NA – Observational study , but with Baseline differences between groups
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA - Observational Study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA -Observational Study
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	(Excluded data described)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	Unclear	Author notes variables known to affect postop delirium risk not included
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Funding not disclosed. Study limitations: -BIS group classifications arbitrary -Time interval not supported by the literature -Retrospective design -Clinical records did not record BIS measuring device -Variables known to affect postop risk not included
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		N = 292 (no intervention groups)
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

### Instructions on rating:

Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •

- <u>Risk of Bias</u>: Based on <u>the criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G1-Chan MT, Cheng BC, Lee TM, et al. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol. 2013;25(1):33-42.

Study	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Characteristics	. openation		mousure	Cutoline	
Chan 2013	N = 1657 screened	n = 450 BIS guided	Delirium assessment:	Delirium was assessed daily in the	Postop complications
China	n = 736 excluded (see	anesthesia group	CAM	mornings after surgery using CAM	BIS vs routine
	below)	(baseline and		criteria based on cog testing (MMSE,	Cardiac:
Settina	N = 921 randomized	Men and women (37.8%)		neuro-psych tests). Inter-rater reliability	28 (6.2) vs 33 (7.3) p=0.13
University Hospital	n = 462 BIS guided	Mean age 68.1±8.2		was not discussed. CAM and MMSE	Respiratory
Shiversity Hospital	n = 80 excluded	Mean age 00.1±0.2		administered at 1 week and 3 month	64 (14.2) vs 81 (17.9) p=0.6
Study Design	8-surgery canceled	BIS group had anesthesia		follow up. Delirium severity was not	Infection
RCT – Double blind	• •	adjusted to maintain a BIS			75 (16.7) vs 104 (23.0)
	4 regional only	value between 40 and 60		discussed.	
Cognitive Dysfunction	6 died before test		Descling characteristics	No similiant difference batures	p=0.02
After Anesthesia	7 refused testing	during maintenance of	Baseline characteristics	No significant difference between	Any complication
CODA Trial)	55 unfit for testing	anesthesia.		groups	48 (10.7) vs 94 (20.8) p=0.0
	n = 459 routine care				
Randomization	n = 58 excluded		Primary outcomes	BIS vs routine care	_
method	4 surgery canceled		POCD at 3 months postop	42/412 (10.2%) vs 62/423 (14.7%),	Comments:
computer-generated	3 regional only			p=0.02	
andom group	4 died before test		Absolute risk reduction	4.5% (0.25-8.9)	The CODA Trial indicated
assignment	5 refused testing		NNT	23 (6-391)	that for every 1000 patients
-	42 unfit for testing				undergoing major surgery,
Study Length/Start-			Secondary outcomes	BIS vs routine care	BIS-guided anesthesia
Stop Dates	Inclusion		Incidence of delirium in hospital	70/450 (15.6%) vs 109/452, p= 0.01	prevented 83 patients from
1/2007 to 12/ 2009	Age >60 yrs		QoR Day 1	11.8±2.1 vs 9.8±2.4 p<0.001	suffering delirium during
	Elective major surgery		QoR Hospital discharge	16.3±1.7 vs 15.3±2.1 p<0.001	hospital admission and 23
Purpose	Duration >2 hrs				patients from POCD at 3
To determine whether	Hospital stay of >4 days		Significant Risk Factors of	N = 902 OR (CI), p	months after surgery.
pispectral index (BIS)-			Postoperative Delirium	Multivariable analysuis	mentile alter eargery:
guided anesthesia	Exclusion		Intraoperative BIS value	0.91 (0.87-0.96) P<0.001	Given that intraoperative lo
decreases the	N = 736		Time with BIS<40 h	2.05 (1.02-4.16) P=0.03	BIS value, long period of
ncidence of post	660 Other research		End-tidal volatile concentration	1.15 (1.05-7.34) P<0.04	deep anesthesia (BIS<40),
operative cognitive	62 MMSE≤ 23			1.13 (1.03-7.34) 1 <0.04	and large doses of
dysfunction (POCD)			Significant Risk Factors of	N = 835 OR (CI), p	anesthetic were predictors
and postoperative	10 refused		Cognitive Dysfunction at 3 mon	Multivariable Analysis	POCD, BIS monitoring with
	4 No reason stated				careful titration of anestheti
delirium in elderly			Age + POCD	1.04 (1.01-1.08), p=0.01	
patients undergoing	Assessments		Delirium	9.58 (4.62-19.9), p<0.001	should prevent unintentiona
major surgery.	1 week before surgery		Intraop BIS value	0.93 (0.85-0.97) p<0.001	deep anesthesia and may b
/ .	1 week after surgery		Time with BIS <40 (h)	1.11 (1.01-1.96) p=0.04	useful for improving
Funding source(s):	3 months after surgery		End-tidal volatile concentration		postoperative cognitive
Competitive	MMSE		(MAC equivalents)	2.31 (1.15-15.6) p=0.03	performance in the elderly.
Earmarked Research	Cognitive failure				
Grant (CUHK4400/	questionnaire	n = 452 routine care group	Delirium assessment:	See above	
06M), Research	questionnaire (CFQ)				
Grants Council of	Verbal fluency test	Men and women (39.6%)	Baseline characteristics		
Hong Kong, and	Chinese auditory verbal	Mean age 67.6±8.3			
Health and Health	learning test	_	Primary outcomes		
Services Research	Color trial	Routine care group had BIS	-		
Fund (04060271).	Quality of recovery (QoR)	measured but not revealed to	Secondary outcomes		
	, , , , , , , , , , , , , , , , , , ,	attending anesthesiologists.	-		
	3 months postop	Anesthesia was adjusted			
Quality Score	Short-Form Health Survey	according to traditional clinical			
6	(SF-36)	signs and hemodynamic			
	(0. 00)	parameters.			
Risk of Bias:		paramotoro.			
High					

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Drop out >10%
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT analysis Very large % of exclusions after randomization and dropouts at 3 month primary outcome analysis
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G1-Radtke FM, Franck M, Lendner J, et. al., Monitoring depth of anesthesia in a randomized trial decreases the rate of postoperative delirium but not the postoperative cognitive dysfunction, Br J Anaesth. 2013; 110 Suppl1:i98-105.

Study	Population	Intervention Groups	Measure	Results Outcome	Exclusions
Characteristics	Fopulation	Intervention Groups	Measure	Outcome	Comments
Radtke F 2013	N = 1277 randomized	n= 575 BIS guided anesthesia	Delirium assessment:	Delirium assessed 2 x day from POD1	n= 45 did not receive
Germany	n = 638 BIS guided	n oro bio guiaca ancoancola	DSM IV	to POD 7 by trained medical personnel	assigned BIS-guided
bermany	n = 45 did not receive BIS	Mean age = 69.7 (6.3)	POCD	supervised by a psychiatrist and delirium	anesthesia
atting			FUCD	experts, all were blinded to tx group.	
etting	guided	Men and Women (44.7%)			n=19 missed canceled surge
Iniversity hospital	n= 639 BIS blinded	ASA PS		Postop cognitive dysfunction (POCD)	n=6 inclusion criteria
	n = 39 did not receive BIS	I and II = 305 (53.0%)		assessed the evening before surgery	n=3 withdrawal of consent
Study Design	blinded intervention	III and IV = 270 (47.0%)		and 7 days and 3 months after surgery:	n= 2 technical difficulties
RCT- Parallel groups	N = 1155 analyzed	Surgical specialty:		<ul> <li>Motor screening test</li> </ul>	n=4 regional anesthesia
	n= 575 BIS guided	General surgery = 275 (47.8%)		- Pattern recognition	n= 2 in prone position
Randomization	n= 580 BIS blinded	Orthopedics = 182 (31.7%)		- Spatial recognition	n= 1 hospital staff
nethod		Urology = 40 (7.0%)		-Attention (choice reaction time)	n= 8 unknown reason
stratification	Inclusion	Gynecology = 64 (11.1%)			n= 18 lost to follow-up
onsecutive patient	- Age ≥60 yr	Other = 14 (2.4%)	Baseline characteristics	No significant differences between	in to look to lonow up
ample randomized	- Elective surgery ≥60 min	MMSE(moon) = 28.8 (1.5)	Dasenne characterístics	groups patients who received	n = 18 lost to follow up
	-General	MMSE (mean) = 28.8 (1.5)		• • •	
ccording to ASA PS	-Abdominal			interventions	n = 11 discharged or
/II vs III/IV) and	-Thoracic	Intervention	Primary outcomes		transferred early
lectronically		Anesthesiologists were allowed to	Postoperative delirium		n = 7 unknown reason
andomized into two	- Vascular	use the bispectral index (BIS) data	incidence	N = 191 (18.8%)	
tudy groups	- Orthopedic	to guide anesthesia		BIS guided (575) v BIS blinded (580)	Comments
	-Otorhinolaryngological		Postoperative delirium, n	95 (16.7%;13.9 to 20%) v 124 (21.4%);	POCD: There was increase
tudy Length/Start-	-Oral & maxillofacial	Blinding: OR coordinator not	%; Cl, p	18.3 to 24.9%), p = 0.036	tendency in the BIS blinded
top Dates	-Gynecological	blinded and scheduled patients	N avg BIS values <20	$3.7 (10.8) \times 5.6 (19.5), p = 0.040$	group (p=0.062), but no
/2009-5/2010	- Urologic al	according to allocation:	Duration of surgery	$164 (98) \times 175 (105) p = 0.055$	correlation for POCD on the
ollow-up until 8/2010	-Informed consent	0			19 <sup>th</sup> POD
0110w-up until 8/2010		-BIS guided anesthesiologists	Multivariate analysis	Significant differences	19 POD
	Exclusion	always used BIS monitoring		Delirium v no delirium	
Purpose	- MMSE score <24	-BIS blinded anesthesiologists	Age	1.096 (1.065 to 1.127), p <0.001	
o assess whether	<ul> <li>Hx Neurologic defects</li> </ul>	never used BIS monitoring	Duration of surgery	1.008 (1.006 to 1.009), p <0.001	
oispectral index (BIS)	-Stroke		MMSE		
guided anesthesia	-Seizures, etc	Both anesthesiologist groups'	% BIS <20	1.027 (1.008 to 1.046) p = 0.006	
ersus routine care	-Pharmaceutical study	qualifications were broadly	Multivariate analysis of	Significant predictors at 3 months	
educes the incidence	participation	comparable in order to avoid a	mortality	postop	
of postoperative	-Not planned for general	possible "investigator bias"	Duration of surgery	1.003 (1.001 to 1.006), p = 0.005	
lelirium in elderly		-a switch between teams was	Delirium	2.048 (1.15  to  3.65)  p = 0.015	
patients.	anesthesia	excluded	ASA PS	1.947 (1.124  to  3.371)  p = 0.017	
aucius	-Language barrier	excluded	A5A1 5	1.347(1.12410(3.371)) = 0.017	
Funding source(s):	Protocol	n=580 BIS blinded anesthesia	Delirium assessment:	See above	n= 39 did not receive
supported by	All patients received pre-,				assigned BIS-blinded
Charite'-	peri- and post-op	Mean age = 70.1 (6.5)			anesthesia
Jniversita"tsmedizin	treatment, as specified in	Men and Women (47.6%)	Baseline characteristics	See above	n= 14 missed canceled
Berlin with additional	the standard operating	ASA PS	Busenne enaracteristics		surgery
unding provided by	procedures (SOPs) of the	I and II = 300 (51.7%)	Brimary outcomes	See above	n= 8 inclusion criteria
	hospital.	III and IV = 280 (48.3%)	Primary outcomes	See above	
spect Medical	nospital.	Surgical specialty:			n= 5 withdrawal of consent
ystems, now		General surgery = 284 (49.0%)			n= 5 technical difficulties
ovidien		Orthopedics = $153 (26.4\%)$			n= 1 regional anesthesia
uality Saara					n=1 died
uality Score		Urology = 63 (10.9%)			n=5 unknown reason
		Gynecology = 61 (10.5%)			n=20 lost to follow-up
lisk of Bias:		Other = 19 (3.3%)			
		MMSE (mean) = 28.9 (1.5)			n = 20 lost to follow up
ligh					n = 9 discharged or
		Intervention			
		BIS monitoring was blinded			transferred early
					n = 1 refused
					n = 10 unknown reason

**Conclusion**: Intraoperative neuromonitoring may change anesthetic management and is correlated with a lower incidence of delirium, possibly by reducing extreme low BIS values. In high 4igk surgical patients this may give the anesthesiologist at hand a possibility to influence one precipitating factor in the complex genesis of delirium.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	Unclear	Unclear due to large % of originally randomized patients who did not receive treatment or were lost to follow up in both groups. Had they been included in analysis there may have been a significant difference in baseline characteristics
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	Unclear	The OR coordinator was not blinded; but it is not clear whether this affected other participants knowledge of allocation
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	All others were reported as blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	>10% exclusion + lost to follow up (those who did not receive the assigned treatment after randomization)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Funded partly by Aspect Medical Systems (now Covidien)
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on <u>the criteria from 1-6 only</u>, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

G2 Larsen KA, Kelly SE, Stern TA, Bode RH, Jr., et al. Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: a randomized, controlled trial. Psychosomatics. 2010;51(5):409-418.

Characteristics         Image: Property (conteringed)         As did daily MMSE and DRS days 1-8; n = 240 intervention n = 250 img obstact to definition to version the 200 intervention n = 250 img obstact to definition to version the 200 intervention n = 250 img obstact to definition the 200 img obstact to definition to definiti	04	Demutation	Internetic Course		Results	
ren 240       N = 465       Simple hip/hene       Delifum assessment:       Delifum assessment:       Co-investigate detarmined if DSM IIR       More and a convext (15, 70%)         get carter       n = 240 intervention       N = 956       Co-investigate detarmined if DSM IIR       No service adverse of the convent (46, 70%)         get carter       n = 48 placeb       intervention       n = 340 ing olenzapine       Provide baseline       Co-investigate detarmined if DSM IIR       No service adverse of the convent (46, 70%)         intervention of n = 48 placeb       intervention of n = 48 placeb       No significant difference for demographic       No significant difference for demogra	Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
AA       n = 2.42 kin intervention       n = 2.62 kin intervention       Simple cohort       Simple cohort <td< td=""><td>arsen 2010</td><td>N = 495</td><td>Simple hip/knee</td><td>Delirium assessment:</td><td>RAs did daily MMSE and DRS days 1-8;</td><td>No serious adverse</td></td<>	arsen 2010	N = 495	Simple hip/knee	Delirium assessment:	RAs did daily MMSE and DRS days 1-8;	No serious adverse
titing ingle center patient       Dropouts (detail in AE) n = 30 intervention a = 40 placebo       Complex inpl/iner replacement ability       DRS-R-86 CAM       CAM       Simple cohord dropout before surgery         TU outside balance       Age > 60 intervention a = 40 placebo       Age > 60 intervention a = 40 placebo       No significant difference for demographic replacement       No significant difference for demographic fewore women (48 %)       Simple cohord dropout before surgery         Age > 60 intervention interventor of dependent cohord proper cohord interventor of dependent cohord proper cohord interventor of dependent cohord proper cohord interventor of dependent cohord interventor cohord interventor intration interation interation interventor interventor interventor i	JSA	n = 246 intervention	replacement	DSM-III-R criteria	Co-investigator determined if DSM IIIR	effects reported but large
titing ing conter       Dropouts (detail in AE) n = 50 intervention n = 45 plotexvention n = 45		n = 252 placebo	n = 207 10 mg olanzapine	MMSE	criteria met	n overall (156, 79%)
adient       n = 3 5 intervention       n = 3 6 10 mg clanzapine       Provide baseline       No significant difference for demographics       -Anote V(22)         1 - double bind       App = 2 5 mg       More and women (48.0%)       Sex       Ferror women (48%)       No significant difference for demographics       -Anote V(22)         1 - double bind       Engles packing       Anote transfer to nursing to market ransfer to nursing staff       No significant difference for demographics       -Anote V(22)         1 - double bind       Provide baseline       No significant difference for demographics       -Anote V(22)         1 - double bind       App = 2 A (6.1)       No significant difference for demographics       -Anote V(22)         1 - double bind       App = 2 A (6.1)       App = 2 A (6.1)       -Anote V(22)       -Anote V(22)         1 - double bind       App = 2 A (6.1)       -Anote V(12)       -Anote V(12) <td>Setting</td> <td>Dropouts (detail in AE)</td> <td></td> <td>DRS-R-98</td> <td></td> <td>. ,</td>	Setting	Dropouts (detail in AE)		DRS-R-98		. ,
udy Design DT – Gubbe blind, seebo controlled     n = 44 placebo     Mon and women (46,1%) Age 2 = 56 Age 4 = 50 fm.     No significant difference for demographic and surgical theracteristics, except	Single center			CAM		Simple cohort dropouts
udy Design DT – Gubbe blind, seebo controlled     n = 44 placebo     Mon and women (46,1%) Age 2 = 56 Age 4 = 50 fm.     No significant difference for demographic and surgical theracteristics, except	npatient	n = 50 intervention	n = 36 10 mg olanzapine	-		
udy Design C - double link seeb controlled     Inclusion Age <85 with postop delinum hx Edective total knee or hp reparation whole - mitaly age <85 with postop delinum hx Edective total knee or hp reparation metal status (MMSE)     Men and women (48.0%) ASA 3 = 39.5%     Characteristics/measures As 3 = 39.5%     No significant difference for demographics Fewer women (48%)     -Surgery cancelled (7 Family pressure (2) Genical error (1) Genical error (2) Genical error (2) -	P		3	Provide baseline		
T - double blind, andomization andomization britos - inclusion     Mean age 73.4 (6.1) Age 2 65 with postop delirum hx Elective total knee or hip epidacement     Mean age 73.4 (6.1) AGA 3 = 39.5%.     AGA 3 = 39.5%.     Sex     Fewer women (48%)    Family pressure (2) Medical advice (2) Circle alerro (2) Medical advice (2)       Staffer family pressure (2) merse stop delirum hx English speaking     After transfer to nursing staffer merse stop delirum staffer family pressure (2) Merse stop delirum staffer merse stop merse stop 	tudy Design		Men and women (48.0%)		No significant difference for demographics	
iacabe controlled     Age ≥ 65 Age ≤ 65 this packing     Age ≥ 65 Age ≤ 65 this packing     Age ≥ 65 Age ≤ 65 this packing     -Drug not given (3) -Drug		Inclusion				
Age -65 with postop delinum hx Enclusted motivation bhots simple xs method - initially stifled into two partice - method states or high register and only signed by computer berky method - combificities consistent for all parties to derivative stoperative procesure erative and for involved with the study derivative procedures consistent for all parties stoperative register.       After transfer to nursing floor -Research asst (RA) obtained inform nursing stifled.       After transfer to nursing stoperative provide informed consent metral status (MMSE) metral sta				Sex		
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op Dates       medication       -binded clinical       Significant differences only       41% vs 30% p. 0.02       -Advanced age         vrpose       comotivitites       Preadmission screening       ASA classification based on medical       comotivitites       -Advanced age       -Advanced age       -Advanced age       -Advanced age         vrpose       evaluate the part of the peri- erative anazphice on the surgery       Preoperative procedures       NNT       4 (Lower incidence of delirium 14.4% vs       -Advanced age						
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07       Preadmission screening ASA classification based on medical comorbidities       data -daily assessments post op days 1-8 (or discharge)       Rehab facility Abnormal labs Use of restraints       59% vs 70% (p not reported))       -Knee replacement surgery         rpose evaluate the pact of the peri- erative ministration of stoperative procedures barbers in involved with postop care administered 5 mg olanzapine or placebo immediately before surgery       Simple hip/knee replacement n = 209 placebo Complex hip/knee replacement n = 43 placebo consistent for all patients there placement n = 43 placebo       Simple hip/knee replacement n = 43 placebo       Delirium assessment: n = 43 placebo       Same as above       No serious adverse effects reported but lar n overall (156, 59%)         Nurses not involved with the study administered with transfer to nursing dif Ci arzapine or placebo more stoperative procedures nat from hospital dif Li Up provided ugs       Delirium Dx Delirium Dx Delirium Dx Delermined by blinded reviewer       Simple hip/knee replacement n = 43 placebo Men and women (60.3%) Men ang e 74.0 (6.2) ASA 3 = 45.3%       Primary outcomes Delirium Secondary outcomes       No significant difference for demographics and surgical characteristics, except More women (60.3%)       Simple cohort dropout before surgery -Anxiety (16) -Surgery cancelled (1 -Family pressure (12) -Drug not given (3) -Mariet (2) -Drug not given (3) -Surgery cancelled (1 -Surgery cancell		medication				
rpose revaluate the pact of the peri- erative ministration of surgery       ASA classification based on medical comorbidities      daily assessments post op days 1-8 (or discharge)       Abnormal labs S.6% vs 0%, p=003       53.6% vs 19.5% p<0.0005				,		
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Delirium Dx Determined by blinded reviewer       dropouts before surget -Anxiety (1) -Surgery cancelled (1 -Family pressure (1)         omments: No ITT analysis. Preoperative misrepresentation in 5 (17.9%) patients who developed delirium in the olanzapine-treated group and 1 (1.2%), may have resulted in alcohol withdrawal in e patients analyzed in this study. The high incidence of abnormally low albumin levels occurred in the olanzapine-treated patients. Olanzapine treated patients also used less narcotic medication ggesting it may have reduced the need for analgesics .	rugs			Secondary outcomes	See above	
Juality Score: 5 sk of Bias: High       Determined by blinded reviewer       -Anxiety (1) -Surgery cancelled (1 -Family pressure (1)         opmments: No ITT analysis. Preoperative misrepresentation in 5 (17.9%) patients who developed delirium in the olanzapine-treated group and 1 (1.2%), may have resulted in alcohol withdrawal in e patients analyzed in this study. The high incidence of abnormally low albumin levels occurred in the olanzapine-treated patients. Olanzapine treated patients also used less narcotic medication ggesting it may have reduced the need for analgesics .         onclusion: Administration of 10 mg of oral olanzapine perioperative vs placebo was associated with a significantly lower incidence of delirium. Olanzapine reduced the incidence of delirium, but no		Delirium Dx				
sk of Bias: High -Surgery cancelled (1 -Family pressure (1) pomments: No ITT analysis. Preoperative misrepresentation in 5 (17.9%) patients who developed delirium in the olanzapine-treated group and 1 (1.2%), may have resulted in alcohol withdrawal in e patients analyzed in this study. The high incidence of abnormally low albumin levels occurred in the olanzapine-treated patients. Olanzapine treated patients also used less narcotic medication ggesting it may have reduced the need for analgesics . ponclusion: Administration of 10 mg of oral olanzapine perioperative vs placebo was associated with a significantly lower incidence of delirium. Olanzapine reduced the incidence of delirium, but no	Quality Score: 5					
-Family pressure (1) pressure	Risk of Bias: High					
omments: No ITT analysis. Preoperative misrepresentation in 5 (17.9%) patients who developed delirium in the olanzapine-treated group and 1 (1.2%), may have resulted in alcohol withdrawal in e patients analyzed in this study. The high incidence of abnormally low albumin levels occurred in the olanzapine-treated patients. Olanzapine treated patients also used less narcotic medication ggesting it may have reduced the need for analgesics .						
e patients analyzed in this study. The high incidence of abnormally low albumin levels occurred in the olanzapine-treated patients. Olanzapine treated patients also used less narcotic medication ggesting it may have reduced the need for analgesics . onclusion: Administration of 10 mg of oral olanzapine perioperative vs placebo was associated with a significantly lower incidence of delirium. Olanzapine reduced the incidence of delirium, but no	ommonte: No ITT an	Alveis Preoperative misrepresentation	in 5 (17.9%) patients who dovo	l loned delirium in the clanzaning t	L treated aroun and 1 (1.2%) may have resulted	t in alcohol withdrawal in
ggesting it may have reduced the need for analgesics . Anclusion: Administration of 10 mg of oral olanzapine perioperative vs placebo was associated with a significantly lower incidence of delirium. Olanzapine reduced the incidence of delirium, but no						
nclusion: Administration of 10 mg of oral olanzapine perioperative vs placebo was associated with a significantly lower incidence of delirium. Olanzapine reduced the incidence of delirium, but no			many low albumin levels occurr	eu in the olarizapilie-treated patie	ants. Oranzapine treated patients also used les	s narcour medication
						ما بد بد بد ما مامانین به از با
						bence of delirium, but not

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Detail on exclusions not reported Large number of post-randomization dropouts
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	0	Unclear	Some secondary outcomes were not reported (perceived pain; narcotic use (specific), hypotension, LOS); Large number of AEs in olanzapine group (156, 79%) vs placebo (156, 59%)
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT analysis Data reporting discrepancies Eli Lily provided drug 1 of first authors funded by Eli Lily
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score • from 0-8, where 8 indicates a high quality article.
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: ٠
  - Low risk of bias: Low risk of bias on all 6 domains
  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G2-van den Boogaard M, Schoonhoven L, van Achterberg T, et al. Haloperidol prophylaxis in critically ill patients with a high risk for delirium. Crit Care. 2013;17(1):R9.

Otaul	Daniel II	Otarita C		Results	
Study Characteristics	Population	Study Groups	Measure	Outcome	Adverse Effects
/an den Boogaard M	N = 476 allocated to	n = 177 Haloperidol prevention	Delirium assessment:	Trained ICU nurses performed Dutch	In haloperidol treatment
2013	intervention / control	group	CAM-ICU (Dutch version)	version of the CAM-ICU at least 3	group
letherlands	n = 177 intervention	<b>5</b> 1	RASS	times daily. inter-rater reliability was	14/177 (8%) adjusted dosage
	n = 299 control	Men and women (35%)	PREDELIRIC score	high	(6%) drowsiness
Setting		Mean age $63 \pm 14$		liigii	12 (7%) stopped haloperidol
	Intervention group	Mean age 05 ± 14	Papalina abaractoristica	Control vs Intervention	
CU of a university	Intervention group	Conceptive notionts concerned	Baseline characteristics		-prolonged QTc-time (n = 9)
ertiary care hospital	N = 2320	Consecutive patients screened	APACHE-II score	20 ± 7 vs 19 ± 6, p=0.06	-signs of Parkinsonism (n = 1)
	n = 2084 excluded	for delirium risk	Admitted with sepsis	64 (21%) vs 53 (30%), <b>p= 0.02</b>	-renal failure (n = 1)
Study Design	-low delirium risk	-PREDELIRIC score >50%	Sedation level (RASS)	-1 (-3 to 0) vs -1 (-3 to 0)	<ul> <li>suspected malignant</li> </ul>
Before/After	-delirium <1 day	-dementia dx	<ul> <li>RASS screening compliance</li> </ul>	93.3% ± 1.2 vs 94.5% ± 0.9	neuroleptic syndrome but late
Observational study	-sustained coma	<ul> <li>alcohol abuse in medical hx</li> </ul>	Haloperidol administering		not confirmed (n = 1)
-	n = non treated patients		- Number of treated patients	225 (75.3%) vs 177 (100%), p	
Selection method	-20 non-compliance	ICU patients with a high risk for		<0.0001	None of the 9 prolonged QTc
All consecutive patients:	-22 prevention	delirium who are treated with	- Number of treated days	5 (2 to 12) vs 5 (3 to 11), p=.23	patients developed any
2008 – 2009 as a control	started too late	haloperidol for preventive	PRE-DELIRIC score	$73 \pm 22$ vs $75 \pm 19$ , p= 0.50	tachyarrhythmia during the
period, 2010 -2011 as a	-5 PREDELIRIC	reason.	Alcohol abuse	41 (14%) vs 20 (11%) p=0.37	prolonged QTc-time period.
	score known too late	1683011.			protoriged QTC-time period.
intervention period		The set black with a stimute	Dementia	5 (2%) vs 2 (1%)	0
	-11 haloperidol	These high-risk patients	<b>_</b> .		Comments:
Study Length/Start-	contraindicated	received intravenous haloperidol	Primary outcomes	Control vs Intervention	When delirium was not
Stop Dates	<ul> <li>-2 inclusion missed</li> </ul>	1 mg/8 h or	CAM ICU screening compliance	90.4% vs 94.5%	detected with the CAM-ICU, b
2/2008 to 2/2009	(alcohol abuse)	-a lower dose of 0.5 mg/8 h	Delirium incidence	225 (75%) vs 115 (65%), p=.01	delirium was suspected based
8/2010 to 8/2011	Age >18 yr	$\geq$ 80 years	Number of delirium free days		on medical and nursing report
	PREDELIRIC >50%	body weight <50 kg,	without coma in 28 days	13 (3 to 27) vs 20 (8 to 27), p = 0.003	patients were additionally
Purpose	history of dementia or	serum creatinine level >150	28-day mortality	36 (12%) vs 13 (7.3%), p=0.03	screened by a delirium expert
To evaluate the ICU	alcohol abuse	µmol/L			according to the DSM-IV
delirium prevention	Haloperidol dosage		Secondary outcomes		criteria.
		serum bilirubin level >50		110 (20 to 250) via 00 (20 to 220)	chiena.
policy/protocol resulted	adjusted or stopped	µmol/L.	hrs on the ventilator	118 (39 to 250) vs 90 (36 to 229) , p=	Determined with a offered a off
in quality improvement of				0.24	Potential side-effects of
relevant delirium	Control group	Intravenous haloperidol			haloperidol were observed or
outcome measures.	N = 2132	prophylaxis was started as soon	length of stay on the ICU	7 (3 to 13) vs 6 (3 to 12), p=.65	when spontaneously reported
	n = 1833 excluded	as it was clear that patients had	length of stay in-Hospital	21 (12 to 41) vs 20 (11 to 31), p= 0.16	and mild extrapyramidal side-
PREdiction DELIRium	-low risk	an increased risk, ranging from			effects may have been misse
Intensive Care score	-delirium <1 day	immediately following ICU	incidence of re-intubation	25 (8%) vs15 (9%), p= 0.51	although daily thorough
(PREDELIRIC).	-sustained coma	admission to 24 hours after ICU	incidence of re-admissions	55 (18%) vs 20 (11%), p= 0.03	physical examination of all
(Intebeen (10)).	edetamed conta	admission.	Unplanned removal tubes/lines	58 (19%) vs 21 (12%), p= 0.02	patients is the usual care in th
Funding source(s):	Other exclusion	aumission.	Delirium subtype:	50 (1570) v3 21 (1270), p= 0.02	ICU.
Not described; authors				20(79/) vo $6(29/)$	100.
,	criteria		- Hyperactive	20 (7%) vs 6 (3%)	Deficients when we not
reported no conflicts of	Not possible to assess		- Hypoactive	81 (27%) vs 33 (19%)	Patients who were not
nterest	patient		- Mixed	124 (41%) vs 76 (43%)	preventively treated according
	Serious auditory or	n = 299 Control group (2008-	Subgroup analysis		to the delirium prevention
Quality Score	visual disorders	2009)	highest risk for delirium	benefit most from the haloperidol	protocol, mostly due to non-
4	Inability to understand	,	0	treatment	compliance, served as an
	Dutch	Men and women (39%)		-	additional control group.
Risk of Bias:	Severe mental disability	Mean age $64 \pm 14$	Non-treated patients during	no demographic differences between	Although this group showed
High	Presence of receptive			the control group and this non-treated	similar patient characteristics
		Listorical ashart many of	the implementation period		the historical control group an
	aphasia	Historical cohort group of		group	
		patients with a determined risk		<b></b>	the prophylactic treated
		of 50% or more for delirium who		The incidence of delirium, unplanned	intervention group, the outcor
		were not treated with haloperidol		removal of tubes and re-admission	measures in this group were
		for preventive reason.		rate was significantly higher and the	comparable with the historica
				number of delirium free days was	control group. This supports t
				significantly lower in the non-treated	beneficial effects of prophylad
				group compared with the treated	treatment with haloperidol.
				intervention group. (See PDF)	L
		hylactic treatment with low dose hald			

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Baseline characteristics had significant differences
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Before-after study Authors discuss possible confounders based on non- compliant previously treated patients
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G2-Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. Anaesth Intensive Care. 2007;35(5):714-9.

Study	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Characteristics		intervention Groups	weasure	Cutcome	Comments
Prakanrattana 2007	N = 126	n = 63 Risperidone 1.0 mg	Delirium assessment:	CAM -ICU rated by trained ICU nurse	Adverse Effects
Thailand	n = 63 risperidone		CAM-ICU	twice daily (between 8 a.m. and 18 p.m)	Adverse Encots
manana	n = 63 placebo	Men and women (42.8%)	0, 111 100	in the ICU and once daily at 18:00 pm	Risperidone vs placebo
Setting		Mean age 61.3 (9.7)		after discharged from ICU; severity and	Significant difference
Jniversity Hospital	n = 27 delirium	Weall age 01.3 (9.7)		inter-rater reliability not described	Tracheal re-intubation: 0 vs 4,
		1 may of view ovidence on		Inter-rater reliability not described	
Study Decima	n = 99 no delirium	1 mg of risperidone or			p=0.019
Study Design	In structure	placebo sublingually when	Deservice and an advantation		No Constitution of all fits and a state
RCT (double-blind,	Inclusion	the patients wake up in ICU.	Baseline characteristics	No significant difference between groups	No significant difference
placebo-controlled)	Age >40 yrs				Renal failure: 2 vs 3, p=1
	undergoing elective		Primary outcomes	Risperidone (63) vs placebo (63)	Respiratory failure: 2 vs 4,
Randomization	cardiac surgery with				p=0.68
method	cardiopulmonary bypass		Incidence of delirium	11.1% vs. 31.7%, P=0.009	Arrhythmia: 6 vs 6, p=1
Computer generated				RR = 0.35, (0.16-0.77);	Re-operation: 2 vs 1, p=1
number	Exclusion			NNT = 4,.85	Cardiovascular instability: 3 vs
	N = not described		Secondary outcomes (NS)		p=1
Study Length/Start-	Underwent emergency		Length of ICU stay	3.3 (2.3) vs 3.2 (1.9), p=0.88	•
Stop Dates	surgery		Length of hospital stay	10.5 (6.1) vs 10.3 (4.4), p=0.574	
Not described	Admitted to ICU before			10.0 (0.1) to 10.0 (1.1), p 0.01 1	Comments:
	arriving at operating room		Risk Factors:	Delirium (27) vs No delirium (99)	The early events after anesthes
Burposo	Pre op delirium		Age	64.2 (6.6) vs 60.2 (10.3), p=0.017	are assumed to be important fo
Purpose			Time from opening eyes to	04.2 (0.0) vs 00.2 (10.3), p=0.017	
To evaluate the	Hx psychiatric problems				developing post op delirium.
potential of			following commands	112.2 (91.8) vs 61.97 (57.4), p=0.002	
isperidone to prevent			NYHA functional class (2/3/4)	13/14/0 vs 7/27/1, p=0.50	Respiratory failure leading to
postoperative delirium			Post op renal failure	4 (14.8%) vs 1 (1%), p=0.007	cerebral hypoxemia may also b
following cardiac			Post op Respiratory failure	5 (18.5) vs 1 (1.0), p=0.002	involved in pathophysiology of
surgery with			Tracheal re-intubation	4 vs 0, p=0.002	post op delirium.
cardiopulmonary			Length of ICU stay	4.7 (3.6) vs 2.8 (1.4), p=0.002	
bypass and the			Length of hospital stay	13.3 (8.4) vs 9.6 (3.8), p=0.004	
secondary objective					
was to explore clinical			Factors associated with	Multiple logistic regression	
factors associated			postoperative delirium	OR (CI), p	
with postoperative			Age	1.04 (0.98-1.09), 0.214	
delirium.			NYHA Functional class	0.289	
			1-2	1.00	
Funding source(s):			3-4	1.73 (0.63-4.77)	
•				1.73 (0.03-4.77)	
Not disclosed			Time from opening eyes to	0.000	
			following commands	0.003	
Quality Score			≤70 min	1.00	
5			>70 min	4.57 (1.66-12.59)	
			Postoperative respiratory failure	13.78 (1.15-165.18), 0.038	
Risk of Bias:			Postoperative renal failure	13.89 (0.99-197.26), 0.052	
Unclear					
		n = 63 placebo group	Delirium assessment:	See above	
		Men and women (39.6%)	Baseline characteristics	See above	
		Mean age 60.7 (9.8)			
		j , , ,	Primary outcomes	See above	
		Identical sublingual placebo			
		not possible: Listerine strip	Secondary outcomes	See above	
		substituted	coordary outcomes		
		Substituteu			
	1	1	1	l he incidence of postoperative delirium. Multi	

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Blinded = patients, investigators, ICU nurses, (person placing sublingual drug or placebo not blinded)
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	Exclusions not described in detail (no CONSORT flow chart)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Funding source not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):	1		BIAS RATING = Unclear
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 5

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G2-Wang W, Li HL, Wang DX, et al. Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: a randomized controlled trial\*. Crit Care Med. 2012;40(3):731-9.

	Population N = 1346 screened	Intervention Groups	Measure	Outcome	Adverse Effects
China	N = 1346 screened				Comments
		n = 229 haloperidol group	Delirium assessment:	Level of sedation assessed using RASS	Adverse effects:
	n = 736 excluded	n = 3 failed to receive study	RASS	(if patient unarousable assessment	No significant difference
	N = 608 eligible	drug (ITT-analyzed)	CAM-ICU	repeated later or noted as comatose.	between groups for adverse
Setting	n = 151 refused			CAM-ICU administered by trained	effects related to delirium
Multicenter (2)	N = 457 randomized	Men 145 (63.3%)		physician daily (from 4:00 PM to 6:00	-Arrhythmia during infusion
ICUs – Tertiary	(included in ITT analysis)	Mean age 74.0 ( 5.8)		PM) in either the ICUs or the general	-change of heart rate-
teaching hospitals.	n = 229 haloperidol	Body mass index: 24.1 (8.0)		wards days 1 – 7. Delirium severity and	corrected QT interval after
	n = 228 placebo			inter-rater reliability were not discussed.	study drugl infusion
Study Design	·	Haloperidol (0.5 mg			-significant heart rate-
RCT (double-blind,	Inclusion	intravenous bolus injection	Baseline characteristics	No significant difference between groups	corrected QT interval
placebo controlled)	>65 yrs	followed by continuous			prolongation after study drug
	ICU admission after	infusion at a rate of 0.1 mg/h	Significant differences for	Haloperidol vs placebo	infusion
Randomization	noncardiac surgery	for 12 hrs	perioperative variables		-episode of extrapyramidal
method	0,1		Mean duration of anesthesia (hr)	5.51 (2.55) vs 4.81 (2.34), p= .003	symptoms
Computer-generated	Exclusion	Postoperative analgesia	Mean duration of surgery (hr)	4.51 (2,.42) vs 3.79 (1.13), p=.001	-RASS at end of study drug
randomization codes	N = 889 (after screening/	routinely included patient-	Median total intra-op infusion (ml)	2700 (2000-4000) vs 2550 (1600-3675),	infusion
	eligibility)	controlled epidural analgesia	1 ( )	p =.048	-time to extubation
Study Length/Start-	311 Non-surgical patients	or patient-controlled			-all cause 28 d mortality
Stop Dates	299 < 65 years	intravenous analgesia.	Primary outcomes		
6/2009 to 5/2010	51 Prolonged baseline	Supplemental	Incidence of delirium within 7 days		Comments:
	QTc	analgesia was administered	after surgery	15.3% vs 23.2% , p =.031	Apart from decreased
Purpose	26 Terminally ill	with fentanyl if necessary	Daily prevalence of delirium		incidence of postoperative
To evaluate the	22 Neurosurgery	, , , , , , , , , , , , , , , , , , , ,	POD1	7% vs 13.2%, p=.028	delirium, it was found that the
efficacy and safety of	18 Visual/hearing	For all patients,	POD 3	1.7% vs 5.3%, p=.041	time to onset of delirium was
short-term low-dose	impairment	multicomponent approaches	Risk for postoperative delirium	OR (CI), p	significantly prolonged (mean,
intravenous	9 Parkinsonism	to reduce risk factors of	· ······ F · ··· F · ···· · · · · · · ·	0.574 (0.352-0.937), p=.026	0.5 day longer) and the
haloperidol for	2 Neuromuscular disease	delirium as suggested by	Efficacy outcomes		number of delirium-free days
delirium prevention in	151 Refused	Inouye et al (1999, 2006)	Time to onset of delirium (hr)	6.2 (5.9–6.4) vs 5.7 (5.4–6.0),p=.021	was significantly increased
critically ill elderly		were included in routine	Number of delirium-free days	6.8 (0.5) vs 6.7(0.8), p= .027	(mean, 0.1 day more) by
patients after	Follow-up	care.	Coma or delirium	15.7% vs 23.7%, p.032	haloperidol prophylaxis.
noncardiac surgery.	For 28 days after surgery		Median length of ICU stay (hr)	19.6 (16.3-22.9) vs 41.4 (39.3-43.5),	
	for postoperative			p.006	Because haloperidol can
Funding source(s):	complications		Coma-free and delirium-free	6.8 (0.7) vs 6.7 (0.9), p=.030	relieve certain symptoms of
Not disclosed	complications		Incidence of non-delirium	0.0 (0.1) to 0.1 (0.0), p=.000	delirium (agitation or
			complications within 7 days	4 (11.4%) vs 16 (30,.2%), p.040	hyperactive symptoms), it is
			Development of non-delirium	+ (11.470) V3 10 (00,.270), p.040	possible that patients
Quality Score			compilations within 28 days	6 (17.1%) vs 19 (35,8%), p=.057	receiving haloperidol might
6				0 (11.170) V0 10 (00,070), p=.001	temporarily have their
5			Subgroup analysis (risk for		delirious symptoms
Risk of Bias:			Delirium)		masked during and
High			Intra-abdominal surgery	14.5% vs 24.7%, p=.018	immediately after the period of
ngn			initia abdominal surgery	14.0% V3 24.7%, p=.010	drug infusion, thus increasing
		n = 228 placebo group	Delirium assessment:	See above	the measure of delirium-free
		n = 228 placebo group n = 1 failed to receive study	Demium assessment.		time.
			Pacalina abaractoristica	See above	une.
		drug (ITT-analyzed)	Baseline characteristics	See above	Limitations
		$M_{00}$ 142 (62 79()	Primary outcomes	Saa ahaya	-no baseline cognitive tests
		Men 143 (62.7%) Mean age 74.4 (7.0)	Primary outcomes	See above	-intraoperative parameters
			Secondary outcomes	Saa ahaya	were different
		Body mass index: 23.5 (3.7)	Secondary outcomes	See above	
		pleashe (permatentias)			-placebo delirium incidence lower than anticipated
		placebo (normal saline)			iower man annopateu
					1
Osnaluaian Essabilit	and and a shart to the factor of		an alanttan an an bida da ata da ta ta	tion of loss door introduce and below of the test	if a sufficient state of the st
	/ patients admitted to intensive /e delirium. The therapy was v		ery, snort-term prophylactic administra	tion of low-dose intravenous haloperidol sign	ificantly decreased the

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences in intraoperative parameters
• Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Significant baseline imbalances Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 6

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains •

G2-Kaneko T, Cai J, Ishikura T, et al. Prophylactic consecutive administration of haloperidol can reduce the occurrence of postoperative delirium in gastrointestinal surgery. Yonago Acta Med. 1999;42(3):179-84.

				Results	1
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
Characteristics Kaneko 1999 Japan Setting University Hospital Study Design randomized, comparative clinical study Randomization method The randomization was conducted by way of a closed envelope system Study Length/Start- Stop Dates 4/1995 to 8/1998	<ul> <li>N = 78 <ul> <li>n = 38 haloperidol</li> <li>n = 40 normal saline</li> </ul> </li> <li>Inclusion <ul> <li>Elective GI surgery</li> <li>Admitted to High and ICU</li> <li>1 or 2 weeks before</li> <li>scheduled surgery</li> <li>Oral consent</li> </ul> </li> <li>Exclusion <ul> <li>N = not described</li> <li>No criteria provided</li> </ul> </li> <li>Post admission testing <ul> <li>Interview</li> <li>Clinical exam</li> </ul> </li> </ul>	Intervention Groups n = 38 haloperidol group 5 mg iv Men/women: 24/14 Mean age 72.4 ± 8.2 5 mg of haloperidol in 1.0 mL intravenously postoperatively at 21:00 for 5 consecutive days	Measure         Delirium assessment:         DSM-III-R         Baseline characteristics         Ischemic heart disease         Hypertension         Respiratory disease         Diabetes mellitus         Liver disease         Cognitive impairment         Primary outcomes         incidence of delirium         Secondary outcomes         Intensity and duration of delirium	OutcomeRAs rated cog test and sleep pattern, delirium were determined if DSM-III-R criteria met on day 5. Inter-rater reliability and delirium severity were not discussed.Haloperidol vs Normal saline N = 38 vs 40No significant difference between groups 5 (13.2%) vs 8 (20.0%) 13 (34.2%) vs 12 (30.0%) 6 (15.8%) vs 4 (10.0%) 9 (23.7%) vs 12 (25.0%) 3 (7.9%) vs 6 (15.0%) 2 (5.3%) vs 4 (10.0%)4/38 vs 13/40 , p <0.05	Adverse Effects No extrapyramidal side effects n = 1 transient tachycardia (haloperidol group)
5 days <b>Purpose</b> To assess the effectiveness and safety of the use of haloperidol for the reduction of postoperative delirium <b>Funding source(s):</b> Not described <b>Quality Score</b>	Laboratory testing	n = 40 normal saline group	average and total time of sleep ratio of sleep time during the day and night Use of haloperidol and flunitrazepam potential confounders for delirium incidence	no significant difference in 2 groups lower during the use of haloperidol higher in haloperidol group No significant difference between groups for postop drugs, method of pain control, hypoxia or infection See above	
4 <b>Risk of Bias</b> : High		Men/women: $26/14$ Mean age $73.1 \pm 9.3$ normal saline intravenously postoperatively at 21:00 for 5 consecutive days	Baseline characteristics Primary outcomes Secondary outcomes	See above See above See above	

**Comments:** This prospective study is the first systematic evaluation of the use of prophylactic administration of intravenous haloperidol to reduce the occurrence of postoperative delirium. The mechanism by which haloperidol reduces the occurrence of postoperative delirium is not clear. Some studies suggest that actions other than the blockade of central dopamine receptors may be responsible for haloperidol's calming effect in patients with delirium.

Conclusion: These results suggest that daily postoperative administration of haloperidol can reduce the occurrence of postoperative delirium safely.

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	Unclear	Not described
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Exclusion criteria not described
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	No ITT analysis Funding not disclosed
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Intervention/control groups <50
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G2-G4-Page VJ, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. Lancet Respir Med. 2013;1(7):515-23.

Cture.	Dopulation	Intervention Crowns		sults	Advarce Effects
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects
age VJ 2013	N = 677 assessed for eligibility	n = 71 haloperidol group	Delirium assessment:	Bedside nurse assessed RASS of	
JK	n = 535 excluded (see below)	1 – lost to follow up	CAM-ICU	–2 to +4, and then performed	Haloperidol vs placebo
		n = 71 analyzed	RASS	CAM-ICU twice during each 12 h	Serious
etting	N = 142 randomized	-		shift with a mini of 4 h.	Apnea post treatment for
CU – general adult	n = 71 haloperidol	Men 37 (52%)			agitation 0 vs 1 (3%)
general addit	n = 71 placebo	Mean age 67.9 (16.5)	Baseline characteristics	No significant difference between	
Study Design		Time from ICU admission to		groups	Fast atrial fibrillation with
RCT (double-blind,	N = 141 analyzed	randomisation: 0.9 (0.91)		groups	hypotension 1 (3%) vs 0
lacebo-controlled)	N - 141 analyzeu		Primary outcomes	Haloperidol vs placebo	
hacebo-controlled)	Inclusion	Treatment was initiated			Readmission to ICU with seps
	Inclusion		Alive, delirium-free, and coma-	5 (0–10) vs 6 (0–11); p=0.53	
andomization	Critically ill patients	within 72 h of admission to	free days in first 14 days	RR: -0.48 (-2.08 to 1.21)	1 (3%) vs 1 (1%)
nethod	≥18 years	ICU.	Secondary outcomes		
ndependent nurse, in	mechanical ventilation within 72 h		Days in delirium in first 14 days	5 (2–8) vs 5 (1–8) p=0·99	Failed extubation 1 (3%) vs 3
:1 ratio, with permuted	of admission	Patients received	Days in coma in fi rst 14 days	0 (0–2) vs 0·5 (0–2) p=0·99	(4%)
lock size of four and		haloperidol 2.5 mg or	Alive, delirium–free,coma-free		
ix, using a centralized,	Exclusion	placebo intravenously every	days in first 28 days	19 (0–24) vs 19·5 (0–25) p= 0·57	Oversedation: 11 vs 6
ecure web-based	N = 535	8 h, irrespective of coma or	Days in delirium in first 28 days	5 (2–10) vs 5 (1–9) p= 0·71	
andomization service	114 expected to be discharged	delirium status.	Days in coma in fi rst 28 days 0	0 (0-2) vs 1 (0-2) p=0.90	QTc prolongation: 7 vs 6
	within 48 h of admission		Ventilator-free ds in first 28 ds	21 (0–25) vs 17 (0–25) p=0·88	
Study Length/Start-	107 declined to participate	The first dose was given at	Mortality at 28 days	20 (28·2%) vs 19 (27·1%)	Drop out: 1 vs 1
Stop Dates	97 moribund, unlikely to survive	either 8 am, 4 pm, or		RR 1.04 (0.61 to 1.77)	
lp to 28 days	more than 48 h	midnight, depending on the	Length of critical care stay	9.5 (5–14) vs 9 (5–18) p=0.47	Reasons for study drug
1/9/2010 to9/21/2012		time of randomisation.	(days)	18·5 (12–31) vs 26 (15–40)	termination:
1/9/2010 109/21/2012	49 undergone uncomplicated	time of randomisation.		p=0.54	2 days CAM-ICU negative
	elective surgery	Ctudy drug was	Length of hospital stay (days)		
Purpose	37 more than 72 h from	Study drug was		No significant difference between	20 (28%) vs 26 (37%)
o establish whether	admission	discontinued on ICU		groups in primary analysis	
arly treatment with	28 QTc more than 500 ms on	discharge, once delirium-			Discharge from ICU
aloperidol would	current ECG	free and coma free for 2			17 (24%) vs 12 (17%)
lecrease the time that	28 already on antipsychotics	consecutive days, or after a	Secondary data analysis	13% (8.75-17.00) vs 20% (17.5-	
urvivors of critical	24 moderate to severe dementia	maximum of 14 days of	RASS ≥ +2	26.75) p=0.0075	Oversedation 8 (11%) vs 5
Iness spent in delirium	or cognitive	treatment, whichever came			(7%)
or coma.	impairment	first.			
	23 structural brain damage				QTc ≥500 msec
unding source(s):	17 language difficulty: learning or	Patients, clinical staff and			7 (10%) vs 4 (6%)
lational Institute for	English language	research staff blinded			Died 5 (7%) vs 4 (6%)
lealth Research	disability	n = 71 placebo group			
	7 Parkinson's disease	1 – lost to follow up	See above	See above	Discontinuation of active
uality Score	6 previously participated in Hope-	1 – discontinued			treatment 3 (4%) vs 7 (10%)
	ICU	n = 70 analyzed			
		II = 70 allalyzeu			14 days after randomisation
	2 haloperidol allergy	Map $4E(649/)$			,
lick of Picc	1 younger than 18 years	Men 45 (64%)			3 (4%) vs 6 (9%)
Risk of Bias:	15 others	Mean age 68·7 (14·9)			
OW		Time from ICU admission to			Extrapyramidal symptoms
		randomisation: 0.88 (0.81)			0 vs 1 (1%)
					Other 8 (11%) vs 5 (7%)
		0.9% saline i.v. same			
		protocol as above			
comments: Defining no	rmal cognitive function as the absence	e of delirium and coma in a pati	ent is an inevitable constraint becau	se it is not possible to be confident in	delineating the cause of coma a
isorder or drugs in many	/ ICU patients. Patients who died with	in 14 days were assessed with	zero delirium-free coma-free days t	o manage the possible conflicting effe	cts of haloperidol on delirium an
				dult respiratory distress syndrome	and a manapartable on adminute an

**Conclusion**: These results do not support the hypothesis that haloperidol modifies duration of delirium in critically ill patients. Although haloperidol can be used safely in this population of patients, pending the results of trials in progress, the use of intravenous haloperidol should be reserved for short-term management of acute agitation.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Low
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 8

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G2-Vochteloo AJ, Moerman S, van der Burg BL, et al. Delirium risk screening and haloperidol prophylaxis program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr. 2011;11(2318):39

Study	Population	Study Groups	Magazina	Results	Commonto
Study Characteristics	Population	Study Groups	Measure	Outcome	Comments
Vochteloo AJ 2011	N = 445	n = 173 high-risk (≥ 5)	Delirium assessment:	Doctors and nursing staff rated delirium	Adverse effects not
Netherlands	n = 67 excluded (RD	group	DSM IV	symptoms during their daily rounds and	described
	score completed	group		assessments	
Setting	incorrectly)	Women 79.2%		(No cognitive testing)	Comments:
Teaching Hospital		Mean age $86.6 \pm 6.5$		(	Multivariable analysis:
	N = 378 evaluated	Other			The RD-score was a
Study Design		Culor	Baseline characteristics	high-risk vs low risk group	significantly contributing
Prospective cohorts	Inclusion	The Risk Model for Delirium	Dementia	51.4% vs 0% RR: 3.44 (2.87-4.12) p< 0.001	variable for delirium,
(Observational study)	Age>65	was designed with a cut-off			length of stay and
, , , , , , , , , , , , , , , , , , ,	Hip fracture	point of 5; patients scoring 5	ASA -III-IV	45.7% vs 22.9% RR: 1.68 (1.36-2.07) p < 0.001	alternative living situation
Selection method	-low energy trauma	or more points were			at 3 months.
A series of consecutive		considered high-risk	Institutional residence	61.8% vs 10.2% RR: 3.17 (2.54-3.95) p< 0.001	
admissions; patients	Exclusion	patients.			Age and ASA
based on Risk Model	N = not described	F	Having no partner	79.3% vs 60.9% RR: 1.74 (1.26-2.41) p< 0.001	classification were strong
for Delirium (RD score)	Hip fracture with	The high risk group was	- · ·		independently contributing
(≥ 5 as a high-risk	pathologic origin	prescribed 1 mg haloperidol	Psychotropic drug use	51.4% vs 24.4% RR: 1.82 (1.47-2.25) p< 0.001	variables as well.
group, and < 5 as a low		2 x day for delirium			
risk group)		prophylaxis	Spinal/epidural anesthesia	97.5% vs 91.1% RR: 2.26 (1.05-4.85) p= 0.006	The RD-score had a
5 - 17					moderate sensitivity
Study Length/Start-	All patients	When patients developed a			(71.6%) and specificity
Stop Dates	prospective evaluation	delirium, they were fully	Primary outcomes		(63.8%)
1/2008 to 12/2009.	At admission	assessed to exclude a	delirium incidence	42.4% vs 14.1% RR: 1.98 (1.62-2.41) p< 0.001	
2005-2007	-standard procedure	somatic cause and treated			The negative predictive
	and recording	by the psychiatric	Secondary outcomes		value (NPV) of a score <
Purpose		department.	Length of stay $\ge$ 10 days	65.1% vs 44.1% RR: 1.61 (1.27-2.05) p< 0.001	was quite high (85.9%),
To determine whether	During follow up				which is very important as
using prophylaxis	-in hospital		Alternative living situation at 3	62.3% vs 17.0% RR: 4.25 (2.65-6.80) p< 0.001	a screening instrument
would diminish delirium	-3 months		months*		should have a high NPV.
incidence in hip fracture	-12 months		In-hospital mortality	5.8% vs 2.0% RR: 1.60 (1.12-2.26) p= 0.050	
patients; and to					The consequence of a
investigate the value of	Risk Model for		3-month mortality	23.1% vs 8.3% RR: 1.69 (1.37-2.10) p< 0.001	false positive test (i.e.
the RD score and	Delirium				prophylactic treatment with
differences between	Predisposing risk factors		12-month mortality	37.0% vs 14.6% RR: 1.77 (1.45-2.17) p< 0.001	low-dose haloperidol in a
low- and high-risk	-delirium during				non-delirious patient) is
patients in delirium	previous hospitalization	n = 205  low- risk (< 5)		prospective (2008-2009) vs historical (2005-	generally modest as very
incidence, length of	-dementia	group	Historical comparison	2007)	few side effects of a low
stay, return to pre-	-clock drawing (small				dose of haloperidol can be
fracture living situation	or big mistakes)	Women 69.3%	age	83.7 vs 82.9 (P = 0.082)	expected.
and mortality.	-Age (70-85; >85) -impaired hearing	Mean age 81.4 ± 7.1			Therefore, its moderate
<b>F</b> (-)	-impaired vision		male	26.2% vs 24.3% (P = 0.515)	positive predictive value
Funding source(s):	-ADL problems	No prophylaxis protocol		070/ 00.00/ ( D. 0.00)	(42.2%) is of lesser
No funding	-use of heroin,		delirium incidence (vs 2005)	27% vs 29.0% ( P = 0.28)	importance.
	methadone or morphine			070/	importance.
Quality Score	-daily consumption of 4		delirium incidence (vs 2006)	27% vs 23.9%, P = 0.81	Delirium was diagnosed
3	or more alcoholic			070/	based on clinical
Risk of Bias:	beverages		delirium incidence (vs 2007)	27% vs 27.8%, P = 0.44	examination, as stated in
	507010903				the DSM IV. However, the
High					author did not use a cog
					test before.
		1	1		

prove to be an accurate tool for identifying high risk patients with poorer outcome regarding delirium incidence, length of stay and return to pre-fracture living situation.

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
Balanced allocation (1 point if achieved):     Description of the method used for balanced allocation in sufficient detail to allow an     assessment of whether it should produce comparable groups. This will typically include     either a valid randomization procedure or prospective individual matching between     intervention and control groups.	0	High	Significant baseline differences Observational study
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Observational study
<ul> <li>Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Patients not eligible due to incorrect RD scoring 67/445 (15%)
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Extreme baseline imbalances Probable confounders (delirium vs cognitive impairment) Historical groups were not scored by RD model
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):	··		BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: **Low** risk of bias: Low risk of bias on all 6 domains ٠

  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
     High risk of bias: High risk of bias on 2 or more of 6 domains

G2 Kalisvaart KJ, de Jonghe JF, Bogaards MJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc. 2005;53(10):1658-66.

Study	Population	Intervention Groups		Sults	Adverse Effects	
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Adverse Effects	
Kalisybaart 2005	N = 430	n = 212 (0.5 mg 3 x day)	Delirium assessment:	Daily rating of CAM and DSM IV		
he Netherlands	n = 212 intervention	n = 179 intermediate risk	DSM-IV	based on MMSE, DRS, digit	Unmasking = 2	
	n = 218  placebo	n = 33 high risk	Confusion Assessment Method	spans	g =	
Setting		n oo nigir nak	(CAM)	DRS for delirium severity	Dropouts n = 20	
ledical school	Inclusion	Men and women (81.1%)	DRS-R-98	Dito for definding seventy	-n = 3 in compliance	
			DK3-K-90			
iffiliated hospital	Age ≥70	Mean age 78.71 (6.04)	Describes also sectorization	l la la marida la cambra a ba	-n = 3 withdrew consen	
	Acute or elective hip surgery	• • •	Baseline characteristics	Haloperidol vs placebo	-n = 11 protocol violatio	
Study Design	Intermediate or high risk for postop	Intervention	measures	No significant difference between	-n = 3 adverse events	
RCT-double blind,	delirium*	Trial medication started on		groups in baseline characteristics		
lacebo controlled		admission and continued until 3 d			Lost to follow up n = 11	
	Exclusion	after surgery	MMSE	No difference between groups		
Randomization	N = 78 (list in PDF)	All patients assessed daily for	Informant Questionnaire on			
nethod	Delirium at admission	efficacy and safety	Cognitive Decline in the Elderly	Minimal both groups	No drug related side	
Systematic screening	No risk factors at admission	Geriatric nurses and geriatricians	Snellen test	Some impairment both groups	effects were seen throug	
of new admissions;	Hx haloperidol allergy	provided proactive geriatric	APACHE II	Overall relatively good clinical	the study period	
equential assignment	Use of cholinesterase inhibitors	consultation on all patients		condition (low scores)		
y computer generated	Parkinsonism	-structured multimodular	Blood urea nitrogen/creatinine	Light dehydration both groups	Adverse events were	
code; research	Epilepsy	protocol (see PDF)	Geriatric Depression Scale	Low both groups	never related to extra-	
eam/participants	Levodopa tx	If postop delirium occurred	Barthel Index	High scores both groups	pyramidal symptoms	
linded; checked by	Profound dementia	-treatment according to	Burther maex	nigh beeree bear groupe	pyramiaar cymptomo	
nterviewing assessors	Language barrier	standard procedures	Primary outcomes (postop		No sedation reported	
iter viewing assessors	Intubation	-haloperidol 3 x d or	days 1-3)		No sedation reported	
tudy Length/Start-	Respiratory isolation	•	Incident delirium	N = 201		
		-lorazepam 3 x d	incident delinum			
top Dates	Aphasia	-or both in increasing doses		Haloperidol vs placebo		
/2000 to 8/2002	Coma	depending on delirium sx		N = 32 vs 36 patients		
Duration 1 to 6 d	Terminal illness	-assessed for severity and		15.1% vs 16.5%		
based on onset of	Delay of surgery >72 h	duration		RR 0.91 (0.59 to 1.44)		
lelirium)	Prolonged QTc interval	In case of emergency:				
	-≥470 ms women	independent physician could	Secondary outcomes (postop			
Purpose	-≥460 ms men	request unmasking	days 1-3)	Haloperidol vs placebo		
o assess the		Adherence recorded daily	Highest delirium rating score	14.4 ± 3.4 vs 18.4 ± 4.3		
effectiveness of 1.5 mg	*Risk Factors	Daily assessments	Mean difference	4.0 (2.0 to 5.8), p <.001		
aloperidol daily versus	Visual impairment worse than	-MMSE	Duration of delirium (days)	5.4 ± 4.9 vs 11.8 ± 7.5		
placebo on the primary	20/70 after correction	-DRS-R-98	Mean difference	6.4 (4.0 to 8.0), p <.001		
incident delirium) and	Severity of illness ≥16	-Digit Span Test	Length of hospital stay	17.1 ± 11.1 vs 22.6 ± 16.7		
econdary	- APACHE II	9.1 open 1 oot	Mean difference	5.5 (1.4 to 2.3), p <.001		
deterioration of	Cognitive impairment ≤24	n = 218 placebo (3 x d)	Delirium assessment:	See above	1	
lelirium) prevention of	-MMSE	n = 181 intermediate risk	Dennum assessment.		Unmasking = 5	
postoperative delirium	Index of dehydration ≥18	n = 35 high risk			onindoking o	
n hip surgery patients.	-ratio of blood urea nitrogen to	n = 2  no risk	Baseline characteristics		Dropouts n = 28	
Thip surgery patients.	creatinine	$\Pi = 2 \Pi 0 \Pi S K$		See above	-n = 4 in compliance	
unding course(a).		Man and waman (70.00()	measures	See above		
Funding source(s):	Intermediate risk	Men and women (78.9%)			-n = 6 withdrew consen	
The medical center	-presence of 1 or 2 risk factors	Mean age 79.57 (6.27))			-n = 7 protocol violation	
unded this study	High risk				-n = 8 adverse events	
	-presence of 3 or more risk	Intervention (see above)	Primary outcomes	N = 194	(not described)	
	factors		See above		-n = 3 randomization	
					violation	
Quality Score = 7	*Low risk patients were assessed		Secondary outcomes			
	daily according to the protocol for		See above		Lost to follow up n = 24	
Risk of Bias = Unclear	incident delirium but received no					
	prophylactic medication					
comments: Haloperidol	patients with delirium continued to have	e significantly lower severity scores	on days 5-8. The findings of the cur	rent study may indicate a "priming" e	ffect (i.e., therapeutic bloor	
	ol were reached sooner once treatmer			tent etady may maloute a primiting e		
		onstrated no efficacy in reducing the	incidence of postoporativo dolirium	It did have a positive offect on the a	everity and duration of	
			Incoduce of costocerative cellulut	I UUU HAVE A DUSHIVE EHECLUH HIE S		

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	1	Low	
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	1	Low	
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	Unclear	High number of dropouts (>10%; 9% Haldol; 13% placebo) 8 adverse events in placebo not described
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	1	Low	Did do ITT analyses; impact unclear
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = Unclear
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 7

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows: Low risk of bias: Low risk of bias on all 6 domains ٠

  - **Unclear** risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - High risk of bias: High risk of bias on 2 or more of 6 domains

G5-Bee Gek Tay L, Chew Chan MP, Sian Chong M. Functional improvement in hospitalized older adults is independent of dementia diagnosis: experience of a specialized delirium management unit. J Hosp Med. 2013;8(6):321-7.

Characteristics         Performance         Delirfum assessments of all measures listed by a trained assessment for method         Early recophlic measures listed by a trained assessment of addressing all precipitating fact addressing all precipitating fact addressing precipitating fact addressing all precipitating fact	Study	Population	Intervention Groups	Measure	Sults Outcome	Comments
Bese Gek Tray L 2013 Singapore         In + 146 m = 24 excluded N = 122 analyzed N = 42 excluded N = 122 analyzed N = 42 excluded N = 42 exclu		ropulation	intervention Groups	Weasure	Outcome	Commenta
SingaporCAMCAMmeasuresmeasuresdetectormeasuresdetectormeasuresdetector		N = 146	n = 82 dementia present	Delirium assessment:	Baseline and daily assessments of all	Farly recognition of
N = 122 analyzed prestMen and ycomen (64.6%) Mean age 84.2 (7.4)Abbreviated Mental Test (AMT) C-MMSE DRS - 99-revfrom the time of admission utill discharge form the GAUaddressing all presciptions addressing all presciptions addressing all presciptions the 24 mission compression free metation metatio	····,···					
etating erating init (GMU) init (GMU) init (GMU) init (GMU) registration (			Men and women (64.6%)			
exercise       n = 4.0 dementia absent       n = 4.0 dementia absent       CAM-sev       Significant differences between groups       groups <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>						
Jnill (GMU)       Inclusion (study Design)       For event admission (SMU core interventions (study Length)       GMU core interventions (structured protocols)       GAM:sev       Significant differences between groups       Significant differences between groups       Bignificant differences groups       Bignificant differ		•	Weall age 04.2 (7.4)		discharge from the Givio	
Linkup Design Trospective schort Prospective schort Age 250Inclusion Age 250CML were proper schort absort admission to CML admission to CML admission to CML etteriaCML core interventions (structured protocols) -ariy mobilization -avoidance of chemical restraints -avoidance of ch		n = 40 dementia absent		-	Cinnificant differences hat were	
Stady Design Prospective cohort       Admitted to greating medicine department admission 16 GMU Admitsed to greating admission 16 GMU Admitsed to greating admission 16 GMU Admitsed to greating admission 16 GMU Admitsed to admission refersion thereing inclusion mething inclusion refersion thereing inclusion refersion therei	. ,			CAM-sev	•	<b>o</b> 1
Prospective cohort         Admitted to geratric medicine department dimission to GAM         -a-avidance of physical restraints in early mobilization         CAM-see Preparticing         4,74 (147) vs 52 (1.71), p.0.07         appart to be imig according to be imig according to be imig according to be imig           Side Cloin method Mericial inclusion inferial cording to CLMM         Exclusion						
Selection endod         medicine department Delinium kat or after anvoidance of physical restraints -avoidance restraints -avoidance of physical restraints -avoidance of physical restraints -avoidance of physical restraints -avoidance of physical restraints -avoidance avoid -avoidance avoidance -						
Salection method meeting inclusion; indria       Delirium dx àt or after admissions (CAM)						
Admissions to GAU retering inclusion riteria       admission (CAM)       if possible - daily review of need for - 1V		•				
retering inclusion ritreira strieria Strieria Study LegtNStri 12010-11/2011 Purpose To examine the findence of a n = 7 respiratory or finection control precutions or oritical n = 7 respet admission roleges of definition Swere a phasia serieritical match comprehensive Swere a phasia serieritical Molical lines equiring special monitoring special do monitoring special di monitoring special do monitoring special di monitoring special						the positive functional
criteria     Exclusion     N = 24     -1/     -1/       Study Length/Start- Stop Dates     n = 7 respiratory or infection control precautions or critical liness equination of delimical precautions or critical liness equination of delimical special monitoring -telementy (afto of NI)     Primary outcomes     All patients (present + absent) 8.2 days     None of the patin addition to compare to compare to precautions or critical liness equination special monitoring -telementy (afto of NI)     None of the patin -therapeutic activities (3 x d) -DT and OT sessions     Primary outcomes     All patients (present + absent) 8.2 days     None of the patin addition       Purpose for examine the program (the Centery (afto of NI) corgarm (the Centery (afto of NI)) corgarm (the Center et patin dementia on program (the Center et patin terring and the center or dependence (1-90)     Primary outcomes     All patients (present + absent) 3.54 (561), p <0.001	Admissions to GMU	admission (CAM)	if possible			outcomes in these
Name BiologN = 24 and 7 respiratory or infection control infection so critical infection so critical <br< td=""><td>meeting inclusion</td><td></td><td><ul> <li>-daily review of need for</li> </ul></td><td>Dementia absent most common</td><td>UTI = 32.9% vs 42.5%</td><td>patients.</td></br<>	meeting inclusion		<ul> <li>-daily review of need for</li> </ul>	Dementia absent most common	UTI = 32.9% vs 42.5%	patients.
Study Length/Star- Stop Dates Stop Dates Purpose To examine the Detention Gontoring Inflector of a multicomponent definition Special monitoring -therapeutic activities (3 x d) -therapeutic activities (3 x d) -therapeut	criteria	Exclusion	-IV			
Study Length/Star- Stop Dates Stop Dates Purpose To examine the Detention Gontoring Inflector of a multicomponent definition Special monitoring -therapeutic activities (3 x d) -therapeutic activities (3 x d) -therapeut		N = 24	-catheter	Primary outcomes	All patients (present + absent)	None of the patient
Stop Dates       infection control      daily orientation (3 x d)      daily orientation (3 x d)       Mathematical data (1, 2, 2, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 0, 0, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 0, 1)       had been subjection (3, 4, 2, 3, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 2, 2, 3, 1, 2, 2, 3, 1, 2, 2, 3, 1, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 2, 3, 1, 2, 2, 3, 1, 2, 2, 2, 3, 1, 2, 3, 1, 2, 2, 3, 1, 2, 3, 1, 2, 2, 3, 1, 2, 3, 1, 2, 3, 1, 2, 2, 3, 1, 2, 3, 1, 2, 2, 3, 1, 3, 1,	Study Length/Start-	n = 17 respiratory or	-supplemental oxygen			admitted to the GMU
11/2010-11/2011       precautions or critical influences      therapeutic activities (3 x d) DT and OT sessions      Comparison						had been subject to
Purpose To examine the influence of a progress of claim monitoring progress of claim monitoring instancial claim content in the study. Progress of claim site of comma thereing the communicate Bevere aphasia severe aphasia instancial claim content in the study. Progress of claim site of thereing the communicate severe aphasia instancial claim site of thanking to flass infinity of Half Calify improvement fraining attending physician y that finding the progress of claim site of thanking to flass infinity of Half claiming improvement site of thanking to flass the site of site of the site of thanking to flass the site of the site of the site of the site of the site of the site of the site of the site of the site of the site of the site of the site of the site of the site of the s	•					
Purpose To examine the mituenco of a multicomone of a terminal alles a severe aphasian = 7 repeat admission multicomone of a multicomone of a multicomone of a total dependence (21-60) severe dependence (21-60) severe dependence (21-60) severe dependence (21-60) severe dependence (100)CMMSE concel multicomone of a total dependence (21-60) severe dependence (91-99) full independence (100)CMMSE concel multicomone of a total dependence (100)This study iack total dependence (21-60) severe dependence (91-99) full independence (100)CMMSE concel multicomone of a concel CAM-sev change B a -2.17 (1.68) vs -3.08 (1.67), p 0.000 NS (0.22 and 0.35) NS (0.00)This study iack total dependence (1.70) resist of BAM admission (by patient, family or geriatrician A ia tensision comprehensive metha a lock and imaging Charission A ia tensision resist of Blas: High-n = 40 dementia absent e a do totake and severity of liness-n = 40 dementia absent abveCall CAM-sev change Prodicars of functional recovery at discharge Predictors of functional recovery a la tests and		•			1.44(2.38) n < 0.001	prijelea reekanti
To examine the multicomponent definition management program (the Geriatin Outonia Dide patients SNU) on functional programs (the Geriatin Outonia Dide patients SNU) on functional programs (the Geriatin Outonia Dide patients SNU) on functional programs (the Geriatin SNU) on functional programs of delinicus shale patients for functional recovery.     -bright (ignt therapy (other sleep enhancement measures) -total dependence (0-20) -total dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -full independence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -moderate dependence (0-1-00) -full independence (0-1-00) -full independence (0-1-00) -moderate dependence (0-1-00) -full independence (1-00) -full independence (1-00) -f						This study lacks data
Influence of a multicomponent delirium management belirium management brogram (the Geriatic Source static binistry of Hear Bases adding and the cords review balance index adding and the cords review balance index adding and the cords review balance index adding and the cords review balance index addin to cord anding and the cords review adding and t			, , ,			
Indition Indition Indition Indition Coma Coma Coma Terminal liness Unable to communicate Severely combative (risk of herentia Dider patients and the functional recovery.Indition indicate dependence (0-20) -severe dependence (0-10)MBI (mean) at discharge Improvement/change at dischargeIndition 2.92 (2.58) vs 5.20 (2.88), p <0.001 +0.61 (1.70) vs 3.15 (2.68), p <0.001 +0.61 (1.70) vs 4.315 (2.68), p <0.001 Hind independence (91-90) -4uli independence (100)Indition patient addition patient CAM sev change Functional outcomes Functional outcomes Progress to less dependent Medical records review DSM-IV criteria for dementia Delirium subtype by geriatrician Medical records review DSM-IV criteria for dementia Delirium subtype by geriatrician *did del records review DSM-IV criteria for dementia Delirium subtype by geriatrician *did del records review DSM-IV criteria for dementia Delirium subtype by geriatrician *did text and imaging Charlson comorbidity index Severity of liness index Modified Barthel Index (MBI)In a 40 dementia absent Meade absent Baseline characteristics Baseline characteristics Baseline characteri				Functional performance gain	1 9 1	
Idelifum management Dorgram (the Geriatric Multion functional SMU on functional orgress of delivious Montoring Unit – SMU on functional on corgress of delivious blace patients and the progress of delivious functional recovery.ComaDementia present vs absent 2.29 (2,58) vs 5.20 (2.88), p <0.001 +0.61 (1.70) vs +3.15 (2.88), p <0.001 +0.61 (1.70) vs +3.15 (2.88), p <0.001 +0.61 (1.70) vs +3.15 (2.68), p <0.001 +1.91 (4.87) vs +6.73 (5.74), p <0.001 High therapy attending physician)In this study, pre existing dementia of delivious blace patients from fur improvement; CAM see vchange Functional outcomes Misitry of Health Quality Score 3Dementia present vs absent 2.29 (2.88), p <0.001 High therapy -2.17 (1.68) vs -3.08 (1.67), p 0.006In this study, pre existing dementia -did not take lo recover from del MBI and MBI change Progress to less dependentDementia present vs absent 2.29 (2.88) vs 1.43 (6.43), p 0.001 High vs 1.43 (6.43), p 0.001 High methia -did not take lo recover from del MBI and MBI change Progress to less dependentDementia present vs absent addition patients Baseline characteristics Primary outcomesDementia present vs absent addition patient Baseline characteristics Primary outcomesIn this study, pre everity of illnessQuality Score 3n = 40 dementia absent efficituan aboven = 40 dementia absent Baseline characteristics Primary outcomesSee aboveSee aboveSee aboveRisk of Bias: -lighn = 40 dementia absent -physical exam -ligh making and			ennancement measures)	MDL (maan) at diasharra		
crogram (the Geriatric Monitoring Unit— Monitoring Unit— Monitoring Unit— Monitoring Unit— Monitoring Unit— Severe aphasia Severe aphasia Dider patients and the amentia on used to communicate Severe aphasia Severe aphas		, , , , , , , , , , , , , , , , , , ,		MBI (mean) at discharge	19.42 (17.1) p <0.001	resolution.
Monitoring Unit – Monitoring Unit – SMU) of functional progress of delirious bider patients and the progress of delirious inctional recovery.Unable to communicate vere aphasia Severely combative (risk of harm to self, staff, others) - slight dependence (91-99) - slight dependence (100)Amt charge - CAM.sev charge - CAM.sev charge - Strotchal outcomes - MBI and MBI change - Progress to less dependentAssessments (slight of the app - Strotchal outcomes - NS (0.022 and 0.35) - NS (0.023)In addition, patie - did not take lo - did not take lo - did not take lo - roduce del - roduce del - roduce del - roduce del - solution a disma - did not take lo - roduce del - roduce del <br< td=""><td></td><td></td><td></td><td></td><td></td><td></td></br<>						
SMU 0 n functional sources of definitions or progress of definitions to bright dependence (21-60) mark to self, staff, others) contraindications to bright dependence (91-99) -slight dependence (91-99) -full independence (100)       AMT change +0.61 (1.70) vs +3.15 (2.68), p <0.001 +1.99 (6.16), p <0.003 +1.99 (6.16), p <0.001						
progress of delirious older patients and the impact of underlying dementia on functional recovery.Severely combative (risk of harm to self, staff, others) Contraindications to bright light therapy functional recovery						existing dementia did
Jole Patients and the gementia on functional recovery.harm to self, staff, others), Contraindications to bright light therapy Refusal of GMU admission (by patient, family or attending physician)					+0.61 (1.70) vs +3.15 (2.68), p <0.001	not preclude delirious
Impact of underlying dementia on functional recovery.Contraindications to bright light therapy Refusal of GMU admission (by patient, family or attending physician)-full independence (100)DRS-sev DRS-sev change CAM-sev change Progress to less dependentB.00 (6.74) vs 14.45 (6.90), p 0.008 -8.17 (7.25) vs -12.05 (6.43), p 0.001 NS (p 0.13)In addition, patie dementia -did not taked madition appear Baseline characteristicsFunding Source(s): Funding Quality Improvement Funding Cognitive eval by geriatrician 3-full independence (100)DRS-sev DRS-sev change CAM-sev change Progress to less dependentB.00 (6.74) vs 14.45 (6.90), p 0.008 -8.17 (7.25) vs -12.05 (6.43), p 0.001 NS (p 0.13)In addition, patie dementia -did not taked of the object -2.17 (1.68) vs -3.08 (1.67), p 0.006In addition, patie dementiaQuality Score 3Assessments (all periatrician Baseline characteristicsDelirium assessment: Baseline characteristicsSee aboveNS (p.0.13)In addition, patie dementiaBighNe (all records review DSM-IV criteria for dementia -beirium subtype by geriatrician At admission -comprehensive med hx -physical exam -lab tests and imaging Charlson comorbidity Index severity of lilnessMedical records review aboveDelirium subtype low abovePolo09 P 0.001Polo03Unable to adjust premorbid functi status at admissMultivariate analysis (all patients) -physical exam -lab tests and imaging Charlson comorbidity Index severity of lilnessPolo01 P 0.003Polo01 P 0.003Polo01 P 0.003Polo03						patients from function
dementia on functional recovery.light therapy Refusal of GMU admission (by patient, family or attending physician)light therapy Refusal of GMU admission (by patient, family or attending physician)In addition, patie CAM sev change CAM sev change Functional outcomes MBI and MBI change Progress to less dependent-8.17 (7.25) vs -12.05 (6.43), p 0.001 NS (p 0.13)In addition, patie dementia -0.17 (1.68) vs -3.08 (1.67), p 0.006Quality Improvement FundingAssessments (all patients) Cognitive eval by geriatrician Medical records review DSM-IV criteria for dementia Delirium subtype by geriatrician Highn = 40 dementia absentDelirium assessment: Baseline characteristics Primary outcomesSee above-8.17 (7.25) vs -12.05 (6.43), p 0.001 NS (0.22 and 0.35) NS (1.00)In addition, patie dementia -did not take ion recover from del -did not appear NS (0.22 and 0.35)Quality Improvement Fundingn = 40 dementia absent Men and women (55%) Mean age 84.0 (8.1)Delirium assessment: Baseline characteristics Primary outcomesSee aboveSee aboveUnable to adjust premorbid functi status at admissi P 0.009Physical exam -ab tests and imaging Charlson comorbidity Index Severity of Illness Index Modified Barthel Index (MBI)GMU core interventions as aboveFemale Hypoactive delirium vs hyperactive delirium Severity of IllnessP 0.001 P 0.003P 0.001 P 0.003In addition ecover from del redictors of functional recovery at discharge	older patients and the	harm to self, staff, others)			+1.99 (4.87) vs +6.73 (5.74), p <0.001	improvement.
functional recovery.Refusal of GMU admission (by patient, family or attending physician)dementia -did not take lo recover from del -did not take lo see aboveNS (p 0.13) -217 (1.68) vs -3.08 (1.67), p 0.006dementia -did not take lo recover from del -did not take lo recover from del -did not take lo see aboveQuality Score 3n = 40 dementia absentDelirium assessment: -did not recover at dischargeSee aboveSee aboveUnable to dijust periodi funct status at admiss <tr< td=""><td>impact of underlying</td><td>Contraindications to bright</td><td>-full independence (100)</td><td>DRS-sev</td><td></td><td></td></tr<>	impact of underlying	Contraindications to bright	-full independence (100)	DRS-sev		
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geriatrician At admission -comprehensive med hx -physical exam -lab tests and imaging Charlson comorbidity Index Severity of Illness Index (MBI)abovePredictors of functional recovery at dischargeMultivariate analysis (all patients)status at admissP 0.009P 0.009P 0.001P 0.001P 0.001P 0.003P 0.003P 0.003P 0.003				Primary outcomes	See above	
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-iab tests and imaging Charlson comorbidity Index Severity of Illness Index Modified Barthel Index (MBI)				Female	P 0.009	
Charlson comorbidity Index Severity of Illness Index Modified Barthel Index (MBI)				Hypoactive delirium vs hyperactive		
Severity of Illness Index Modified Barthel Index (MBI)		-lab tests and imaging		delirium	P 0.001	
Severity of Illness Index Modified Barthel Index (MBI)						
Modified Barthel Index (MBI)						
(MBI)						
		(MBI)				
		(MBI)				

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences between groups at admission
<ul> <li>Evidence that balance was achieved</li> </ul>			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – prospective cohort
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA – prospective cohort
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Baseline significant differences Unclear possible confounders
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		Dementia absent = 40
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

### G5-Eeles E, Thompson L, McCrow J, Pandy S. Management of delirium in medicine: experience of a Close Observation Unit. Australas J Ageing. 2013;32(1):60-3.

Study	Population	Intervention	Results				Comments
Characteristics			Measure		Outcome		
Eeles E 2013 Setting Hospital – general	N = 175 2010 (usual care control)	Usual care -admission from ED -general medical ward -management by ward staff		2010 7/2010-11/2010 N = 175	2011 7/2011-11/2011 N = 237 n = 132 no COU	<b>COU</b> <b>n = 105</b> n = 100 delirium dx	A dedicated unit, with advantages o continuity of care, may share more
nedicine and special unit Study Design	<b>N = 237 2011</b> n = 132 usual care n = 105 COU	-5 RNs -1 nursing assistant (AIN) -delirium with risky behavior = 1:1 AIN	Delirium assessment: COU only CAM	Retrospective review of coding in	(usual care)	Nurse assessment using CAM and PAS (>2) at study	features with preventive approaches.
Dbservational: before and after design	Inclusion Diagnosis of delirium (CAM) Score >2 on PAS	Close Observation Unit (COU) -conversion to 4 bed unit -trained AINs (full day)	Pittsburg Agitation Rating Scale (PAS)	medical chart		entry	Using standard measures to attem to identify those immediately at
Historical controls from chart review; 2011	-agitation -aggression	-Nurse educator = trainer -definitions for delirium and	Age (mean SD)	79.6 (11.1)	80.0 (10.4)	80.3 (11.3)	greatest risk (through falls and
prospective cohort based on inclusion	-vocalization -resistiveness	dementia -environmental considerations	Gender (women)	51%	51%	43%	neuropsychiatric disturbance) and
criteria	Falls score >21	-communication styles -practice partnership models of	Mean LOS (SD)	24.7 (36.0)	21.7 (39.5)	22.7 (28.5)	proactively managing these
<b>Purpose</b> To develop and evaluate a new model	Inclusion (2010 controls) ICD-10 diagnostic	-operations of COU	Falls in hospital n (%) Yes No	n = 165* 5 (3.0%) 160 (97.0%)	n = 187* 6 (3.0%) 181 (97.0%)	3 (3.0%) 102 (97.0%)	problems ameliorates the proximal threat
of care for the management of patients with delirium who are at risk to	code for delirium dx Admitted to internal medicine services	COU staffing -RN oversight -AIN 1:4 patients (continuous)	Died in hospital n (%) Yes No	n = 165* 25 (15.0%) 140 (85.0%)	n = 187* 10 (5.0%) 177 (95.0%)	7 (7.0%) 98 (93.0%)	The weak sensitiv and specificity suggests that
themselves through behavioral or osychiatric disturbance	<b>Exclusion</b> N = not described Primary dx of a	COU protocols -hourly behavioral observations -Pittsburgh Agitation Scale	Discharged home n (%) Yes	n = 172* 133 (77.0%)	n = 187* 152 (81%)	80 (76.0%)	concordance between case- finding methods is
Funding source(s):	mental health problem	(PAS) -Pain Assessment in Advanced	No	39 (23.0%)	35 (19.0%)	25 (24.0%)	far from ideal.
Not described Quality Score		Dementia Scale (PAADS) -targeted nursing interventions -toileting	Diagnosis of delirium (retrospective coding)	58%			Studies of delirium should also try and measure, and
3 <b>Risk of Bias</b> : High		-nutrition -diversion activity -mobility -reduced stimuli -patient environment adapted	Diagnosis of delirium ( <i>prospective</i> )			86% Sensitivity 58% Specificity 86%	screen for, dementia.
		-wall clock -orientation reminders -patient biography -safer environment changes	Reduction in mortality p = 0.002	n = 165* 15.0%	n = 187* 5%		
		-high/low profile beds -split rails -height adjustable arm chairs Discharge -falls risk to low or moderate -absence of neuropsychiatric	*NOTE: reported n different than reported total (See Table 1, PDF)				
		disturbance (PAS = 0) for 24 h					

163

#### RATING WORKSHEET

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	Authors indicate no significant difference between COU cohort and historical controls, but there was a significant difference in mortality (p = 0.002) Data did not differentiate between baseline and outcomes
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	NA – observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA-observational study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	2011 usual care' n for some reported outcomes differed from original N; withdrawals/dropouts not discussed
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Before/after design Historical controls Funding source not specified
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above 7. Validated delirium measure used (indicate which measure) (1 point if used):			BIAS RATING = High
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article.
- <u>Risk of Bias</u>: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:
  - Low risk of bias: Low risk of bias on all 6 domains
  - Unclear risk of bias: High or unclear risk of bias on 1 or more of 6 domains
  - **High** risk of bias: High risk of bias on 2 or more of 6 domains

G5-Flaherty JH, Steele DK, Chibnall JT, et al. An ACE unit with a delirium room may improve function and equalize length of stay among older delirious medical inpatients. J Gerontol A Biol Sci Med Sci. 2010;65(12):1387-92.

31009				Outcome	Commonte
Study Characteristics	Population	Study Groups	Measure	Outcome	Comments
Flaherty JH 2010	N = 355 admissions	n = 104 No Delirium	Delirium assessment:	Trained geriatrician administered the CAM within	In a multivariate analysis
USA	n = 207 excluded		Modified CAM (administered	the first 24 hrs of admission (8:00 am - 3:00 pm.)	controlling for the covariates
	N = 148 met inclusion	Men and women (73%)	by 3 geriatricians and unit	After admission, trained nurses performed modified	age, gender, Charlson
Setting	criteria	Mean age 83.2 (7.1)	nurses)	CAM daily on days 1-6. Correlation between	Comorbidity Index, APACHE
Community-based				physician CAM and nurse CAM (r =.56, p <.001).	score and LOS, the ADL
hospital with an			(modified CAM = Inouye	Nurse performed CAMs yielded an intra-class	interaction effect remained
academic university		All patients admitted to the	1999)	coefficient of 0.65 and an alpha coefficient of 0.91.	statistically significantly.
affiliation	Inclusion	ACE Unit	,	'	, , , ,
	Age ≥65		Baseline characteristics	No significant difference between groups	For the finding that patients
Study Design	CAM within 24 hours of				with delirium improved
Retrospective	admission (performed by				function, there are at least tw
observational study	a physician)		Primary outcomes	No delirium vs delirium	explanations.
observational study	length of stay >48 h		prevalence of delirium	16.2% (24/148)	explanatione.
Selection method	Admission from		delirium incidence	16.1% (20/124)	First, delirious patients had a
Convenience sample				10.170 (20/124)	lower mean ADL score on
•	-emergency		Secondary outcomes	No Dolirium vo dolirium	
patients admitted to	department		Secondary outcomes	No Delirium vs delirium	admission, which allowed thi
the ACE Unit during	-clinic		ADL, (admission to		group the room to improve.
the specified time	-directly from home.		discharge, mean SD)	7.4 (4.7) to 6.9 (4.5) vs 4.1 (4.6) to 6.1 (3.9) <.001	
frame					Second, it is possible that wi
	Exclusion		Admitted from home but		delirium, patients either lose
Study Length/Start-	N = 207		discharged to a facility	23 (11/48) vs 40 (6/15) p=.197	function due to the delirium of
Stop Dates	Length of stay <48 h				nurses assessing ADL status
1/ 2008 to 4/2008	Transfer from another		LOS	5.9 (3.6) vs 6.4 (3.1) p=.461	give these patients a lower
4 months	floor				score because of the deliriur
	Transfer from ICU		LOS,log10-transformed	0.71 (0.23) vs 0.76 (0.21), p=.281	
Purpose	CAM not performed				Then, as the delirium
To compare delirious	within 24 h of admission		Died, % (n)	1.9% (2) vs 4.5% (2), p=.582	improves, so do ADL scores
patients with non-			, ()		
delirious patients on					
an Acute Care of the	Data source	n = 44 Delirium	Delirium assessment:	See above	Limitations
Elderly (ACE) Unit	Included patients'				-not clear which part of the
with a Delirium Room	medical charts reviewed	Men and women (68%)	Baseline characteristics	See above	ACE unit or DR or both, coul
(DR) related to	3 individuals (1 study	Mean age 85.3 (5.7)	Dasenne characterístics		have led to a benefit
specific outcomes	author)	Mean age 03.3 (3.7)	Primary outcomes	See above	-ACE Unit principles may
	Standardized form	All potionts admitted to the	Primary outcomes	See above	
including change in function from		All patients admitted to the	Secondamy autoanaa	See above	have had an effect of deliriur
function from	developed by 2	ACE unit, but not all	Secondary outcomes	See above	management
admission to	investigators	delirious patients were			-there is cross-over in
discharge, hospital	No blinding	placed in the Delirium			nursing staff between the Ur
length of stay and		Room during their hospital			and the DR
mortality.	Other Variables	stay.			-use of a convenience
	ADLs (assessed by				sample may have introduced
Funding source(s):	nurses)	43% spent at least some			selection bias
Not disclosed	Calculated from chart	time in the Delirium Room			-the study may have been
	review:	-of these, 47% spent their			underpowered to detect a
	-Acute Physiology and	entire hospitalization in the			significant difference in some
Quality Score	Chronic Health	DR			of the outcomes of interest
3	Evaluation score	-31%spent 50% to <100%			-there was not a control
	(APACHE)	in the DR			group of patients with deliriu
Risk of Bias:	-Charlson Comorbidity	-21% spent <50% in the			
High	Index scores (CCMI)	DR			
			1	I discharge among patients with delirium compared with the second sec	L

165

<b>Evidence Ratings</b> [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> <li>Evidence that balance was achieved</li> </ul> </li> </ol>	0	High	No significant baseline differences but no matching between groups
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Retrospective observational study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	Retrospective observational study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Study design – historical cohort Possibility of selection bias noted by authors Funding not described
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	0		n = 44 Delirium group
TOTAL QUALITY SCORE (0-8)	5		QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •

G5-Lu JH, Chan DK, O'Rourke F, et al. Management and outcomes of delirious patients with hyperactive symptoms in a secured behavioral unit jointly used by geriatricians and pyschogeriatricians. Arch Gerontol Geriatr. 2011;52(1):66-70.

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N =actionts with hyper- active symptoms dmitted to the periatric/psycho- ueriatric Unit (direct dmission from the EmergencyN = $N = 1$ Rec befo befo n = 2 durin n = 3			5		acute medical
Lactive symptoms admitted to the geriatric/psycho- udmission from theRec befo n = 2 durin n = 2 $n = 2$ $n = 3$	22		Length of stay		
$\begin{array}{llllllllllllllllllllllllllllllllllll$				25.5 (20.4) vs 17.3 (14.7), OR 8.3, p = 0.011	deterioration
$\begin{array}{llllllllllllllllllllllllllllllllllll$	covery from delirium		Duration of delirium	21.7 (19.9) vs 10.6 (11.5), OR 11.1, p <0.001	-nursing staff are dua
geriatric Unit (direct durir admission from the n = 2 Emergency n = 8	ore admission		Recovery from delirium	40.7% vs 58.8%, OR 0.4, p = 0.047	qualified in medical and
admission from the $n = 2$ Emergency $n = 8$	2 delirium developed		Mortality	1.9% vs 1.5%, OR 1.3, p = 0.889 (NS)	psychiatric conditions
Emergency n = 8	ring hospitalization				<ul> <li>-the physical structure</li> </ul>
	12 hypoactive delirium		Significant changes for		of the Unit enables close
	8 no psychomotor		indirect admission patients		and persistent
	turbance		after transfer	Before vs after transfer to Unit	observation of delirious
ransferred from other			One-to-one nursing care		patient with hyperactive
	oidance of		reduced	12 (24.1%) vs 1 (1.9%), p = 0.002	symptoms (especially
,	servational bias		Falls reduced	14.2 vs 6.7 per 1000 delirium patient days	psychomotor agitation)
<i>i</i>	ta collector was a visiting		i allo roddood		allowing early
9	ctor with no clinical	n = 68 direct admission	Delirium assessment:	See above	intervention and
	olvement	from ED	Demilan assessment.	See above	management of risk
	olvement		Bacalina abarastaristica	See above	U U
between the two	iformity of the data	Man and	Baseline characteristics	See above	factors
	iformity of the data	Men and women (67.6%)	Dula and a second	On a share	-the secure area
	lection process	Mean age 81.0 (6.9)	Primary outcomes	See above	prevents wandering an
• • • •	andom 20 sets of notes	Hyperactive delirium (80.9%)			reduces the need for 1
	re counter-checked by 2	Residing at home (61.8%)			nursing care
	ependent geriatricians	Dementia (41.2%)			
	d a senior research	Wanderer (57.4%)			
	nager to ensure accuracy	Charlson Comorbidity Index			
	d consistency of	1.8 (1.3)			
	erpretation of the clinical	· · ·			
data		Patients admitted directly to			
Risk of Bias:		the Unit within 24 h of			
High		presentation			
3		p. 550 mailon			

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	No significant difference between study groups, but no matching
o Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	Unclear	Attempts were made to avoid observational bias in data collection
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	0	High	NA-retrospective study
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	Unclear	Historical study groups Investigators reported analyzing data to control for potential bias in the study design/ confounders Funding not described
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	1		
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 4

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias:Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias:Low risk of bias on all 6 domainsoUnclear risk of bias:High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias:High risk of bias on 2 or more of 6 domains ٠

G5-Goldberg SE, Bradshaw LE, Kearney FC, et al. Care in specialist medical and mental health unit compared with standard care for older people with cognitive impairment admitted to general hospital: randomised controlled trial (NIHR TEAM trial). BMJ. 2013;347:f4132.

Ctudy	Population	Intervention Crowns	Na.a	Results		
Study Characteristics	Population	Intervention Groups	Measure	Outcome	Comments	
Goldberg SE 2013	N = 884 randomized (10	n = 310 specialist unit	Delirium assessment:	Not described (reported in text/table, but	What this study	
JK	randomized twice)		DRS-R-98	not described	adds:	
	n = 437 specialist unit	Men and women (56%)	21101100		Best practice acute	
Setting	n = 437 standard care	Median age 85 (80-88	Baseline characteristics	Significant differences between groups	hospital managemen	
Jniversity Hospital –	Excluded after randomization	Median age 00 (00-00	Dasenne characteristics	Specialist (310) vs standard care (290)	of older people with	
		Madical and mantal baalth unit	Cara homo regident			
Combined medical	n = 130 specialist unit	Medical and mental health unit	Care home resident	28% vs 21%, p 0.03	delirium and dementi	
ind mental health	n = 147 standard care	28 bed specialist unit	Median DRS score	19 (11-27) vs 20 (14-27) p 0.03	does not improve	
nit for older people	(See Figure 1 in PDF for detail)	Core protocols = geriatric medical ward	Categorical delirium (DRS >17.75)	53% vs 62%, p 0.02	health status or redu use of hospital	
Study Design	Inclusion	5 enhanced components	Previous paralysis or		resources.	
RCT	Age ≥65	1 specialist mental health staff	hemiparesis	4% vs 10%, p 0.01		
	Identified as "confused" by	-3 nurses	Previous hip fracture	14% vs 7%, p o.01	The experience of	
andomization	physician at admission	-1 occupational therapist			patients and	
nethod	Family member or other carer	-2 x week psychiatrist consultant	Primary outcomes	Significant differences between groups	satisfaction of family	
dentified in acute	available to participate	-additional physiotherapy, speech	Process of care	P <0.05 on 42/132 intervention process	carers, however, are	
dmission unit;	Informed consent	and language therapy	1100033 01 0010	items (See PDF Table 2)	improved	
,					Improved	
ncluded patients	-patient if capacity present	-3 healthcare assistants (activities)	Davis an extent of hereig	(See PDF Table 3)		
andomized 1:1 to	-carer if capacity not present	2 staff trained in recognition and	Days spent at home	NS median 51 vs 45 days, p 0.3	As many of these	
ntervention/control		management of delirium and	Return home from hospital	NS 74% vs 70%, p 0.54	patients are	
roups using a	Exclusion	dementia and person-centered	Overall mortality	NS 22% vs 25% p 0.89	approaching the end	
omputerized log;	N = 277 (see PDF)	dementia care	Move to care home	NS 29% vs 28% p 0.30	of their lives, these a	
linded clinical staff	Critical care required	3 program of organized therapeutic	Readmissions	NS 32% vs 35%, p 0.31	important outcomes	
ut research staff not	Surgery required	and diversionary activities				
linded	Stroke admitting diagnosis	4 environment made more	Secondary outcomes	See PDF Tables	Limitations	
	Patients admitted to medical	appropriate for people with cognitive	-	Table 4: (n = 46 vs 44) Non participant	-compromises in tri	
Study Length/Start-	wards not randomly allocated	impairment		observer study data report on outcomes on	design may have	
Stop Dates	, <b>,</b>	5 proactive and inclusive approach		the limited number of observations	introduced bias	
7/2010 – 12/2011	Protocols – all patients	to family carers was adopted		Table 5 (n = 234 vs 228) Satisfaction	-patients were	
Purpose	Standard medical care			outcomes are reported many of which are	recruited and /or	
To evaluate the	Standard mental health services	Discharge letters to family doctors		significant	excluded after	
combined medical	Rehabilitation	and other community services		Table 6: 90 day follow up outcomes	randomization	
		and other community services				
ind mental health	Intermediate and social care			provide a number of significant	-significant baseline	
init (specialist unit)	No use of physical restraints	Delirium prevention actively initiated		comparisons, but it is not clear how many	imbalances	
o determine		for known risk factors		were in the follow up groups	-limited patients	
mproved outcomes,	Data collection/ assessments				available for follow u	
xperience, and	Trained researcher (s)	n = 290 standard care	Delirium assessment:	See above	-some data was	
atisfaction	interviews				missing	
compared with	Medical and nursing notes	Men and women (49%)	Baseline characteristics	See above		
tandard care	DEMQOL	Median age 85 (80-89)				
	EuroQoL EQ-5D	<b>C</b> ( )	Primary outcomes	See above		
unding source(s):	Charlson Comorbidity Index	Standard care (control)	5			
JK National Institute	Medication history	5 acute geriatric medical wards	Secondary outcomes	See above		
or Health Research	Dementia care mapping (2	6 general internal medicine wards	eccondury outcombe			
Grant	trained researchers)	o general internal medicine wards				
Jian	-observations every 5 minutes	Geriatric medical wards				
Vuelity Coore	for 6 h per patient					
uality Score		-comprehensive geriatric				
	Process of care assessed	assessment				
	-2 senior geriatricians	-staff had general experience with				
lisk of Bias:	Blinded RAs completed	delirium and dementia				
ligh	outcome assessments	-mental health support provided on				
	Follow up = carer interviews 90	request from consulting psychiatrists				
	(7) days after randomization					
	Other – see PDF p 3 of 12					

Evidence Ratings [adapted based on Cochrane risk of bias (top 6 items only), Jadad scoring and Lancet review approach Inouye et al]	Quality Score 1 or 0 [include notes for any 0s]	Risk of Bias Rating (Low; Unclear, High) [include notes on interpretation]	Notes for 0 Quality Scores and Risk of Bias Interpretation
<ol> <li>Balanced allocation (1 point if achieved):         <ul> <li>Description of the method used for balanced allocation in sufficient detail to allow an assessment of whether it should produce comparable groups. This will typically include either a valid randomization procedure or prospective individual matching between intervention and control groups.</li> </ul> </li> </ol>	0	High	Significant differences between groups at baseline
• Evidence that balance was achieved			
<ul> <li>Allocation concealment (1 point if achieved):         <ul> <li>Description of method used to conceal the allocation in sufficient detail to determine whether the intervention allocations could have been foreseen before enrollment by either investigators or participants. Typically, this will be blinded enrollment.</li> </ul> </li> </ul>	0	High	Blinding variable according to role in study
<ul> <li>Blinded outcome assessment (1 point if achieved):         <ul> <li>Description of methods used to blind study participants, investigators, and outcome assessors as to the study group.</li> </ul> </li> </ul>	1	Low	Outcome assessors described as blinded
<ul> <li>4. Completeness of outcome data (1 point if achieved):         <ul> <li>Description of study attrition (withdrawals, deaths and dropouts), and any exclusions from the analyses. Reasons for all such attrition/exclusions should be reported.</li> </ul> </li> </ul>	0	High	Exclusions after randomization (>30%) Acknowledged missing data
<ul> <li>5. Selective outcome reporting (1 point if achieved):         <ul> <li>All primary and secondary outcomes are reported. No evidence that one or more outcomes were not reported, or that additional outcomes (not pre-specified) are reported.</li> </ul> </li> </ul>	1	Low	
<ul> <li>6. Other sources of bias (1 point if achieved): <ul> <li>Problematic study design (historical controls, or before-after study)</li> <li>Extreme baseline imbalances</li> <li>Drug company sponsorship of study (or author(s) disclosed drug company relationship(s)</li> <li>For observational studies: confounders inadequately controlled</li> <li>For RCTs: lack of intention-to-treat (ITT) analysis: HIGH risk of bias if not present</li> </ul> </li> </ul>	0	High	Significant baseline imbalances Exclusions after randomization No ITT
OVERALL RISK OF BIAS (Low, Unclear , High) based on 1-6 above			BIAS RATING = High
7. Validated delirium measure used (indicate which measure) (1 point if used):	0		DRS is validated but no description of delirium assessment
8. Sample size ≥50 each study arm (1 point if achieved):	1		
TOTAL QUALITY SCORE (0-8)			QUALITY SCORE = 3

- Quality score: Give one point for each of the 8 criteria above, where 0=bias or goal not achieved; 1=no bias or goal achieved (or score unclear). Each article should be assigned a score from 0-8, where 8 indicates a high quality article. •
- Risk of Bias: Based on the criteria from 1-6 only, give a Cochrane rating of bias, as follows:oLow risk of bias: Low risk of bias on all 6 domainsoUnclear risk of bias: High or unclear risk of bias on 1 or more of 6 domainsoHigh risk of bias: High risk of bias on 2 or more of 6 domains •