Appendix J: Health economics appendix

Summary of included studies

Two studies aimed at the prevention of delirium in a hospital care setting, one aimed at treatment in hospital setting, and one aimed at prevention in long term care. Two studies were multi-component interventions (Rizzo 2001, Pitkala 2008), one was single component, non-pharmacological intervention (Robinson 2002), and one was a pharmacological intervention (Bracco 2007). There was one randomised controlled trial (Pitkala 2008), two non-randomised controlled trials (Rizzo 2001, Bracco 2007) and one before and after study (Robinson 2002). Multivariate analysis was done in two studies (Rizzo 2001, Bracco 2007). Two studies were carried out in the USA, one in Australia, one in Finland and one in Canada. None of the studies took a UK NHS and personal social services perspective and none measured health benefits in QALYs. All of the studies reported costs and outcomes separately. None of the studies discounted future costs and outcomes appropriately and none carried out a robust sensitivity analysis on the results of an economic analysis. As we found no published economic evaluations that were directly applicable, it was decided that an original economic evaluation should be developed to determine the cost effectiveness of the interventions considered in this guideline.

1 Table J1. Characteristics of included studies

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Author (Year): Pitkala 2008 Country: Finland (government funded health care) Funding: Lions Organization, Helsinki University Central Hospital, Helsinki City, the Academy of Finland Type of analysis: Cost-effectiveness	Study design: RCT Time horizon: 1 year Discounting: None Perspective: Finnish, Helsinki city hospital, resources valued at average unit costs Cost year: 2001	Consecutive delirium patients above 68 years admitted to the general medicine services. Life expectancy was predicted to be above 6 months.	Intervention: Comprehensive geriatric assessment at baseline, atypical antipsychotics were used if necessary, effective general treatments; after acute phase of delirium, patients not recovering from impaired cognition underwent detailed diagnostics of dementia and thereafter received acetyl cholinesterase inhibitors. Comparator: Received usual care. What constituted usual care was not exactly described	1) Mortality rate 2) HRQoL 3) Cost (per patient) incurred in the intervention and usual care arms	1) I:35%, C:30%, n=87, p=0.52 2) Patient's reported HRQoL, I:0.68 (SD 0.12), C:0.62 (SD 0.15); p=0.02 Intervention improved mental function, usual activities, vitality, depression and speech 3) I: €19,737; C:€19,557 (this were based on the use and unit cost of the following health services: primary hospitals, specialized hospitals, specialist consultations, psychiatrist hospitals, nursing homes, long-term care hospitals, skilled home nursing)	Mortality rate was not an adjusted estimate, and health status was measured with an ordinal scale
Primary details	**Design**	**Patient**	**Interventions**	**Outcome measures**	**Results**	**Comments**

		characteristics				
Author (Year): Rizzo (2001) Country: USA Funding: National Institute on Aging, in-kind support from the Claude D. Pepper Older Americans Independence Centre. One of the authors was a recipient of a Midcareer Award from the National Institute on aging and a Donaghue Investigator Award from the Patrick and Cathering Weldon Donaghue Medical research Foundation Type of analysis: Cost-effectiveness	Study design: Non-randomised intervention study Time horizon: Unclear. Study participants enrollment period was 3 years Discounting: None Perspective: Hospital health care provider Cost year: 1995	70 year old patients (and those older than 70 years) with no evidence of delirium but who had intermediate or high risk of delirium	Intervention: multi-component intervention (Hospital Elderly Life Program) Comparator: Usual hospital care	1) Incidence of delirium 2) Mortality rate 3) Additional Cost (per patient) of intervention 4) Non-intervention costs 5) Overall net cost	1) Intermediate risk patients: I:6.5%,C:11.7%,p<0.5; High risk patients: I:18.5%,C:23.5%,NS; Overall:I:9.9%, C:15.0%,p<0.5 2) I:1%,C:2% 3) Intermediate risk patients: I:$564(SE 25),C:$0; High risk patients: I:$662(SE 38),C:$0; Overall:I:$592(SE 21),C:$0 4) Intermediate risk patients: I:$6,124(SE337),C:$7,565(SE$545); High risk patients: I:$7,414(SE$665),C:$6,618(SE $468); Overall:I:$6,484(SE 307),C:$7,300(SE $414) 5) Overall:I:$7,076, C:$7,300	Study was in a single hospital only and was not a randomised trial.
Primary details	**Design**	**Patient characteristics**	**Interventions**	**Outcome measures**	**Results**	**Comments**

Author (Year): Bracco (2007) Country: Canada Funding: Not stated Type of analysis: Cost-effectiveness	Study design: Non-randomized clinical trial Time horizon: Not clear Discounting: None Perspective: Not clear Cost year: Not clear	Patients who underwent cardiac surgery	Intervention: Use of thoracic epidural anaesthesia for cardiac surgery. Patients received 5ml test dose of 1.5% lidocaine with 1:200,000 epinephrine which was given through an epidural catheter. The block was loaded with 6 to 8 ml of 0.125% or 0.25% bupivacaine. Anaesthesia was induced with propofol (1-2mg/kg), fentanyl (2-4µg/kg), or sufentanil (0.2-0.5µg/kg) and rocuronium (0.6mg/kg) Comparator: No use of thoracic epidural anaesthesia for cardiac surgery. Anaesthesia was maintained with intravenous opioids (up to 10-15µg/kg of fentanyl), benzodiazepines (5-10mg midazolam), and sevoflurane (1-1.5 MAC)	1) Incidence of delirium 2) Mortality rate 3) Additional Cost (per patient) of intervention	1) Post-operative delirium complication rate. I:4/506, C:20/787, p<0.02, RR:0.31(95%CI 0.11 to 0.90) 2) ICU Mortality. I: 2/506, C: 14/787, p<0.04, RR: 0.22(95%CI 0.05 to 0.97). Low overall mortality incidence 3)$82	Large sample size, however, cost estimates were not based on clearly described resource use, no sensitivity analysis
Primary details	**Design**	**Patient characteristics**	**Interventions**	**Outcome measures**	**Results**	**Comments**
Author (Year):	Study design:	Older adult	Intervention:	1) Additional Cost of	1) Cost of colourful cups and	There was no

Robinson (2002) Country: USA Funding: The Retirement Research Foundation Type of analysis: Cost-effectiveness	before-and-after non-randomised study Time horizon: Intervention occurred within 5 weeks. Data collection occurred 2 weeks before and after intervention Discounting: None Perspective: Not clear. Intervention materials were purchased from retail shop Cost year: Not clear	patients in a nursing home	Hydration program (to improve dehydration) which included a hydration assistant, an individualized plan of care incorporating the most effective techniques to administer fluid, a colourful beverage cart with colourful pitchers and glasses to enhance residents' interest in drinking, and a choice from 4 beverages at each encounter. Goal was for each resident to consume an additional 8-ounce beverage mid-morning and mid-afternoon, which would increase fluid intake to 1.5L daily Comparator: Use of usual gray coloured institutional carts, white foam cups and limited variety of beverages	intervention 2) Cost savings due to the prevention of associated negative outcomes by intervention	assorted beverages was $3 per resident per week and average cost of employee time per resident per week was $8 2) $103 (p=0.05) per resident per week	measure of delirium incidence or severity, mortality or HRQoL

Table J2. Assessment of the applicability of included studies

Guideline topic: Delirium	**Rizzo 2001; Clinical Question no: c1-10**	**Pitkala 2008; Clinical question no: c3-16**	**Bracco 2007; Clinical question no: c1-8**	**Robinson 2002; Clinical question no: c4-19**
Section 1: Applicability (relevance to specific guideline review question(s) and the NICE reference case1) [Yes/ Partly/ No /Unclear /NA]				
1.1 Is the study population appropriate for the guideline?	Yes	Yes	Yes	Yes
1.2 Are the interventions appropriate for the guideline?	Yes	Yes	Yes	Yes
1.3 Is the healthcare system in which the study was conducted sufficiently similar to the current UK NHS context?	No	Partly	Partly	No
1.4 Are costs measured from the NHS and personal social services (PSS) perspective?	No	No	No	No
1.5 Are all direct health effects on individuals included?	No	No	No	No
1.6 Are both costs and health effects discounted at an annual rate of 3.5%?	No	No	No	No
1.7 Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	No	No	No	No
1.8 Are changes in health-related quality of life (HRQoL) reported directly from patients and/or carers?	No	Yes	No	No
1.9 Is the valuation of changes in HRQoL (utilities) obtained from a representative sample of the general public?	No	Yes	No	No
1.10 Overall judgement: Directly applicable/Partially applicable/Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

[1] As detailed in the 'Guide to the methods of technology appraisal' (June 2008), box 5.1 (page 30). Section 5.2.3 of the guide states: 'There may be important barriers to applying reference-case methods. In these cases, the reasons for a failure to meet the reference case should be clearly specified and justified, and the likely implications should, as far as possible, be quantified.'

Table J3. Excluded studies and reasons for exclusion

Publication	Reason for exclusion
Beaupre 2006	Intervention is a complex clinical pathway with many components that were specifically developed for patients with hip fracture. It is not clear which components are aimed at reducing the incidence of delirium so the use of this evidence for the guideline population as a whole is limited.
Heyman 1995	Cost of intervention was not included
Caplan 2007	Sample size is too small
Pandharipande 2007	The intervention drug studied is neither licensed nor widely used in the UK
The Medical and Health Research Council of The Netherlands, 2007	Still an ongoing Dutch study. Study abstract has no results reported
Rubin 2006	This study was not a comparator controlled study. The study design was weak and a controlled comparison exists elsewhere in the literature (Rizzo 2001).
Webster 1999	The number of participants in one of the study arms is less than 20
Caplan 2006	Study compared the effect of delivering services at two different settings. Comparison was between two areas of rehabilitation namely, home rehabilitation and in-hospital rehabilitation.

Reference List for health economic studies

Beaupre, L. A., et al. "Reduced morbidity for elderly patients with a hip fracture after implementation of a perioperative evidence-based clinical pathway." Quality and Safety in Health Care 15.5 (2006): 375-79.

Bracco, D., et al. "Epidural anaesthesia improves outcome and resource use in cardiac surgery: A single-center study of a 1293-patient cohort." Heart Surgery Forum 10.6 (2007): 301-10.

Caplan, G. A., et al. "Does home treatment affect delirium? A randomised controlled trial of rehabilitation of elderly and care at home or usual treatment (The REACH-OUT trial) (DARE provisional record)." Age and Ageing 35 (2006): 53-60.

Caplan, G. A. and E. L. Harper. "Recruitment of volunteers to improve vitality in the elderly: the REVIVE study (DARE provisional record)." Internal Medicine Journal 37 (2007): 95-100.

Heyman, E. N. and B. A. Lombardo. "Managing costs: the confused, agitated, or suicidal patient." Nursing Economics 13.2 (118): 107-11.

Pandharipande, P. P., et al. "Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial." JAMA 298.22 (2007): 2644-53.

Pitkala, K. H., et al. "Multicomponent geriatric intervention for elderly inpatients with delirium: effects on costs and health-related quality of life." Journals of Gerontology Series A-Biological Sciences and Medical Sciences 63.1 (2008): 56-61.

Rizzo, J. A., et al. "Multicomponent targeted intervention to prevent delirium in hospitalized older patients: what is the economic value (DARE structured abstract)." Medical Care 39 (2001): 740-52.

Robinson, S. B. and R. B. Rosher. "Can a beverage cart help improve hydration?" Geriatric Nursing 23.4 (2002): 208-11.

Rubin, F. H., et al. "Replicating the hospital elder life program in a community hospital and demonstrating effectiveness using quality improvement methodology (DARE structured abstract)." Journal of the American Geriatrics Society 54 (2006): 969-74.

Webster, J. R., et al. "Improving clinical and cost outcomes in delirium: Use of practice guidelines and a delirium care team." Annals of Long-Term Care 7.4 (1999): 128-34.

Health economic literature searches

Table J4: Search terms used in the Medline literature database

No.	Search terms
1	deliri$.ti,ab.
2	(acute adj2 (confusion$ or "brain syndrome" or "brain failure" or "psycho-organic syndrome" or "organic psychosyndrome")).mp.
3	(terminal$ adj restless$).mp.
4	toxic confus$.mp.
5	delirium/
6	confusion/
7	or/1-6
8	*psychoses, alcoholic/ or *alcohol withdrawal delirium/
9	*Substance Withdrawal Syndrome/
10	8 or 9
11	7 not 10
12	limit 11 to (english language and humans)
13	limit 12 to yr="1994 - 2008"
14	13 and economics/QoL filter

Table J5: The economics and quality of life filter

	Search History
1	exp "Costs and Cost Analysis"/
2	economics/
3	exp Economics, Hospital/
4	exp Economics, Medical/
5	exp Economics, Nursing/
6	exp Economics, Pharmaceutical/
7	exp "Fees and Charges"/
8	exp Budgets/
9	ec.fs.
10	(economic$ or pharmacoeconomic$ or price$ or pricing$ or cost$ or budget$).ti,ab.
11	(value adj2 (money or monetary)).ti,ab.
12	(expenditure not energy).ti,ab.
13	or/1-12
14	((metabolic or energy or oxygen) adj1 cost$).ti,ab.
15	13 not 14
16	exp Quality-Adjusted Life Years/
17	quality adjusted life.tw.
18	exp "Quality of Life"/
19	value of life/
20	(qaly$ or qald$ or qale$ or qtime$).tw.
21	disability adjusted life.tw.
22	daly$.tw.
23	health status indicators/

24	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
25	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
26	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
27	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
28	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
29	(euroqol or euro qol or eq5d or eq 5d).tw.
30	(hql or hqol or h qol or hrqol or hr qol).tw.
31	(hye or hyes).tw.
32	health$ year$ equivalent$.tw.
33	health utilit$.tw.
34	(hui or hui1 or hui2 or hui3).tw.
35	disutili$.tw.
36	rosser.tw.
37	quality of well?being.tw.
38	qwb.tw.
39	willingness to pay.tw.
40	standard gamble$.tw.
41	time trade off.tw.
42	time tradeoff.tw.
43	tto.tw.
44	or/16-43
45	15 or 44

Supplementatry tables for health economic model (Chapter 1~~0~~6)

Table J6: Content of the structured geriatrics consultation*

Module / Recommendation	Recommended n (%)
1. Adequate CNS oxygen delivery:	
a) Supplemental oxygen to keep saturation > 90%, preferably > 95%	18 (29%)
b) Treatment to raise systolic blood pressure > 2/3 baseline of > 90mmHg	4 (6%)
c) Transfusion to keep hematocrit > 30%	57 (92%)
2. Fluid / electrolyte balance:	
a) Treatment to restore serum sodium, potassium, glucose to normal limits (glucose < 300mg/dl, <16.5mmol/L for diabetics)	23 (37%)
b) Treat fluid overload or dehydration detected by examination or blood tests	30 (48%)
3. Treatment of severe pain:	
a) Around-the-clock acetaminophen (1 gram four times daily)	25 (40%)
b) Early-stage break-through pain: low-dose subcutaneous morphine, avoid meperidine	13 (21%)
c) Late-stage break-through pain: oxycodone as needed	3 (5%)
4. Elimination of unnecessary medications:	
a) Discontinue / minimize benzodiazepines, anticholinergics, antihistamines	42 (68%)
b) Eliminate drug interactions, adverse effects, modify drugs accordingly	13 (21%)
c) Eliminate medication redundancies	8 (13%)
5. Regulation of bowel / bladder function:	
a) Bowel movement by postoperative day 2 and every 48 hours	42 (68%)
b) D/c urinary catheter by postoperative day 2, screen for retention or incontinence	44 (71%)
c) Skin care program for patients with established incontinence	2 (3%)
6. Adequate nutritional intake:	
a) Dentures used properly, proper positioning for meals, assist as needed	35 (56%)
b) Supplements: 1 can Ensure,** 3 cans Ensure* for poor oral intake	22 (35%)
c) If unable to take food orally, feed via temporary nasogastric tube	1 (2%)
7. Early mobilization and rehabilitation:	
a) Out of bed on postoperative day 1 and several hours daily	36 (58%)
b) Mobilize / ambulate by nursing staff as tolerated, such as to bathroom	18 (29%)
c) Daily physical therapy; occupational therapy if needed	1 (2%)

Module/Recommendation	Recommended n (%)
8. Prevention, early detection, and treatment of major postoperative complications:	
a) Myocardial infarction / ischemia - electrocardiogram, cardiac enzymes if needed	21 (34%)
b) Supraventricular arrhythmias / atrial fibrillation - appropriate rate control, electrolyte adjustments, anticoagulation	3 (5%)
c) Pneumonia / chronic obstructive pulmonary disease - screening, treatment, including chest therapy	27 (44%)
d) Pulmonary embolus - appropriate anticoagulation	31 (50%)
e) Screening for and treatment of urinary tract infection	32 (52%)
9. Appropriate environmental stimuli:	
a) Appropriate use of glasses and hearing aids	3 (5%)
b) Provision of clock and calendar	0 (0%)
c) If available, use of radio, tape recorder, and soft lighting	0 (0%)
10. Treatment of agitated delirium:	
a) Appropriate diagnostic workup / management	1 (2%)
b) For agitation, calm reassurance, family presence, and /or sitter	2 (3%)
c) For agitation, if absolutely necessary, low-dose haloperidol 0.25 - 0.5mg every 4 hours as needed; if contraindicated, use lorazepam at same dose	12 (19%)

* Taken from Marcantonio 2001, ** Ensure is the trade name of a nutritional supplement

Table J7: Risk factors targeted in the Inouye study (1999), the materials used and instructions in the intervention group of the study, and the anticipated NHS resources required to apply the intervention protocol to NHS patients

Targeted Risk Factors	Materials and instructions	Which extra NHS resources?	Which NHS resources are assumed to be available?
1. Cognitive Impairment a. Orientation protocol b. Therapeutic-activities protocol	Board with names of care-team members and day's schedule; communication to re-orientate to surroundings 3 x daily Cognitively stimulating activities 3 x daily (e.g. discussion of current events, structured reminiscence, or word game)	1) Standard word game	1) Board, pens 2) Time resources for reorientation related communication
2. Sleep Deprivation a. Non-pharmacological sleep protocol	At bedtime, warm drink (milk or herbal tea), relaxation tapes or music, and back massage, once daily	1) Relaxation tapes or music	1) Warm drink 2) Resources for back massage 3) We did not account for unit-wide noise-reduction strategies
b. Sleep enhancement protocol	Unit-wide noise-reduction strategies (e.g. silent pill crushers, vibrating beepers, and quite hallways) & schedule adjustments to allow sleep (e.g. rescheduling of medications and procedures), once daily		4) Time resources for adjustments to allow sleep

Targeted Risk Factors	Materials and instructions	Which extra NHS resources?	Which NHS resources are assumed to be available?
3. Immobility Early mobilization protocol	Ambulation or active range of motion exercises 3 times daily. Minimising use of immobilising equipment (e.g. Bladder catheters, physical restraint)		1) Time resources for mobility enhancement resources
4. Visual Impairment Vision protocol	Visual aids (e.g. glasses or magnifying lenses) and adaptive equipment (e.g. large illuminated telephone key pads, large prints books, fluorescent tape on call bell), with daily reinforcement of their use		1) Large print books are already available 2) Time resources for daily reinforcement
5. Hearing Impairment Hearing protocol	Portable amplifying devices, earwax disimpaction & special communication techniques, with daily reinforcement of these adaptations		1) Time resources for earwax disimpaction, special communication techniques and daily reinforcement
6. Dehydration Dehydration protocol	Early recognition and volume repletion (e.g. encouragement of oral fluid intake)		1) Dehydration prevention protocol is included in usual care

1 Table J8: Key Hospital Elder Life Program Staff ‡

Role	Description
Elder Life Nurse Specialist (Master's prepared nurse with training and experience in geriatric nursing)	* Performs daily nursing assessment on all enrolled patients, rounds daily with staff nurses, and conducts the Elder Life nursing interventions that particularly focus on preventing cognitive and functional decline, encouraging mobility, limiting immobilizing medical equipment (restraints, Foley catheters), and reviewing medication lists for psychoactive medications
	* Provides educational activities for nursing staff, including daily one-on-one bedside teaching, informal small group educational sessions, frequent bulletin board updates, monthly newsletter and monthly continuing education in-services on geriatric nursing issues; serves as an educational resource and as a role model for geriatric nursing care
	* Conducts interdisciplinary rounds held twice a week to review all patients in the program, and follows up to assure implementation of recommendation from these rounds
	* Communicates recommendations for interventions and medication changes to the physician staff on a daily basis
	* Serves as a liaison to nursing and other health care specialities in the hospital
	* Assists with discharge planning and assuring communication with community agencies for care after discharge on an as-needed basis (e.g., visiting nurse associations, meals-on-wheels, assisted living, and nursing homes).
Elder Life Specialist / Volunteer Coordinator (Bachelor's prepared [master's preferred] in human services or a healthcare-related field, with geriatric experience, supervisory experience, and excellent communication and organizational skills)	* Unique role created for the Hospital Elder Life Program, combining responsibilities for program operations, interventions, and volunteer coordination
	* Screens all older patients within 48 hours of admission and enrolls appropriate patients into the program; develops an individualized care plan of Hospital Elder Life Program interventions for each patient
	• Conducts program interventions and assures that all volunteer interventions are completed; records and tracks all intervention adherence and program outcome variables; and participates in rotating on-call schedule to assure weekend and holiday coverage
	* As volunteer coordinator, recruits (in collaboration with hospital volunteer services), trains, and schedules all volunteers for the program; creates volunteer assignments on a daily basis (assigning patients and interventions); tracks volunteer adherence with all interventions and intervenes for any adherence problems; provides ongoing volunteer feedback, support, and quarterly performance reviews; creates volunteer newsletter; and runs volunteer educational / support groups

Role	Description
Geriatrician (Board-certified in geriatric medicine, with at least 2 years of experience in geriatric practice including acute care experience)	* Provides geriatric medicine expertise and back-up to the Elder Life nurse specialist and staff
	* Participates in the twice-weekly Hospital Elder Life Program interdisciplinary rounds
	* Provides targeted consultation to the nurse specialist, Elder Life Specialists and floor nurses on geriatric issues, and serves as liaison with the medical staff on an as-needed basis
	* Offers geriatric consultations on Hospital Elder Life Program patients when requested by the patient's attending physician
	* Provides education for the physician staff on geriatric issues through formal lectures, rounds, and one-on-one interaction
Program Director (This role may be assumed by the geriatrician, nurse specialist, or Elder Life Specialist and provides overall leadership for the program)	* Oversees and supervises the entire program, verifies that all interventions are being fully and consistently implemented, holds regular staff meetings, ensures staff performance, and implements and monitors all quality improvement procedures
	* Tracks the program budget and timeline, prepares progress reports for the hospital and funders, and monitors pertinent program outcomes

‡ Inouye 2000