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SYSTEMATIC REVIEW

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Cost-effectiveness of clinical interventions for delirium: A systematic literature review of economic evaluations

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Abstract

Objective: Little is known about the economic value of clinical interventions for delirium. This review aims to synthesise and appraise available economic evidence, including resource use, costs, and cost-effectiveness of interventions for reducing, preventing, and treating delirium.

Methods: Systematic review of published and grey literature on full and partial economic evaluations. Study quality was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).

Results: Fourteen economic evaluations (43% full, 57% partial) across nine multicomponent and nonpharmacological intervention types met inclusion criteria. The intervention costs ranged between US$386 and $553 per person in inpatient settings. Multicomponent delirium prevention intervention and the Hospital Elder Life Program (HELP) reported statistically significant cost savings or cost offsets somewhere else in the health system. Cost savings related to inpatient, outpatient, and out-of-pocket costs ranged between $194 and $6022 per person. The average CHEERS score was 74% (±SD 10%).

Conclusion: Evidence on a joint distribution of costs and outcomes of delirium interventions was limited, varied and of generally low quality. Directed expansion of health economics towards the evaluation of delirium care is necessary to ensure effective implementation that meets patients' needs and is cost-effective in achieving similar or better outcomes for the same or lower cost.

KEYWORDS

cost-effectiveness, delirium, economic evaluation, intervention, quality of evidence, review

1 | INTRODUCTION

Health services worldwide have been increasingly challenged to provide safe and high-quality care for a growing number of patients at risk of delirium and ensure this care is also cost-effective for the most prudent use of finite health care resources.[1] With delirium affecting at least one in four hospitalised older people[2,3] and over

two-thirds of people admitted to an intensive care unit (ICU),[4,5] related care is a significant responsibility of hospital services. Delirium causes complications related to increased morbidity,[6] persistent functional decline,[7] mortality,[8] and signals an increase in frailty.[9] As a result, delirium is associated with high health and social care costs.[10] For example, in the United States (US) alone, the cost of inpatient delirium was estimated as high as 82.4 billion per year (in 2019 US$).[10]

Over the past few decades, progress has been made in understanding the epidemiology of delirium. This includes the demographic and clinical risk factors of delirium and the development of various delirium screening tools,[4,11] best practices and interventions.[12–17] Clinical guidelines make several recommendations for interventions to reduce delirium incidence and duration and optimise recovery in various healthcare settings.[18,19] While current evidence and guidelines[18,19] did not support pharmacological interventions,[14,15] non-pharmacological interventions, particularly multicomponent, demonstrated reduced delirium incidence and severity in at-risk hospital inpatients.[4,16,17,20]

Despite the growing body of clinical research in delirium, economic evidence on resource use, cost and cost-effectiveness, which is critical to value-for-money considerations, remains less understood.[10,21] The impact of delirium interventions on a joint distribution of costs (resource use) and outcomes (beneficial and adverse effects) remains unclear.

Clinical research on the effectiveness of intervention alone is insufficient evidence. An intervention may effectively meet people's needs, but it is not cost-effective to achieve similar outcomes at a greater cost.[22] There is a clear societal and economic imperative to identify and deliver interventions that are not only effective in reducing delirium occurrence but can demonstrate cost-effectiveness.

1.1 | Aims of the study

This article is the second in a series of two reviews examining economic evidence in delirium care to support well-informed healthcare decisions. In the first review, we systematically identified and appraised the methodological quality of research on the cost of delirium; discussed challenges and opportunities for more precise estimates.[10] The primary aim of the current review was to synthesise and appraise economic evidence, including resource use, costs, and cost-effectiveness of interventions for reducing, preventing, and treating delirium.

Significant outcomes

- Findings highlight sparse and low-quality economic evidence of interventions for delirium.
- Insufficient evidence about the factors determining the cost-effectiveness of delirium interventions, such as models of care and target populations.
- To ensure that resource use to reduce, prevent and treat delirium has maximum benefits, economic evaluations should become an integral part of clinical trials, implementation studies, and quality improvement initiatives.

Limitations

- We took a systematic approach to include only English language studies where the key concept (delirium) was clearly defined.
- Despite using a binary system to review and assign quality scores to each study based on the CHEERS adapted checklist, some subjectivity may have biased the scoring.
- Heterogeneity prohibited meta-analysis due to the lack of reported standard error/deviation of mean costs and outcomes.

2 | METHODS

2.1 | Design

A systematic review was registered in the PROSPERO database (CRD42020188487) and reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[23]

2.2 | Search strategy

Using the PICO (population, intervention, control, and outcomes) method,[24] an experienced librarian searched for economic evaluations (full or partial) of interventions for reducing, preventing, and treating delirium (PICO), which reported a change-in-cost or cost-effectiveness information as a primary or secondary outcome (PICO). Using Drummond's classification methods, economic evaluations could be classified as full or partial evaluations. Full economic evaluations are the comparative

analysis of alternative courses of action regarding their costs and outcomes.[22] This differs from partial economic evaluation, which considers costs and outcomes, but either does not involve comparing alternative interventions or relating costs to outcomes.[22] Due to the investigative nature of this review, we included evidence from both full and partial economic evaluation studies and placed no limits on Population (PICO) or Comparator (PICO). Studies that did not evaluate an intervention, conference abstracts, posters, and those not in the English language were excluded. Studies on Delirium Tremens (i.e., delirium caused by alcohol withdrawal) were excluded due to different clinical aetiology and interventions.[25]

Eligible studies were identified by searching six electronic databases in June 2020 and reference list searches. The search was applied to Embase (including EMTREE terms), MEDLINE (including MESH terms), PsychInfo, PsycARTICLES, Econlit and The National Health Service (NHS) Economic Evaluation Database. Additional grey literature was identified using Google Advanced Search. Each database was searched using the core concepts and search terms relevant to "delirium" and "cost" (refer to Table A1).

Search results were imported into EndNote X7 software, duplicates removed, and imported into Covidence online software. Two investigators (Layla Edwards and Irina Kinchin) independently applied the eligibility criteria and documented reasons for exclusion. Any discrepancies were flagged through the platform and resolved through discussion.

BOX 1 The Cochrane-adopted levels of evidence for healthcare interventions. Adapted from AD.Oxman Checklists for review articles. BMJ 1994;309:648–51.[27]

Level I. For a randomised controlled trial, the lower limit of the confidence interval (expressed as a range) for a measure of effect is still above a meaningful benefit in healthcare terms.

Level II. For a randomised controlled trial, the lower limit of the confidence interval (expressed as a range) for a measure of effect is less than a meaningful beneficial effect in healthcare terms; but the point estimate of effect still shows effectiveness of the intervention.

Level III. Measures of effectiveness are taken from non-randomised studies of groups of people where a control group has run concurrently with the group receiving the intervention being assessed.

Level IV. Measures of effectiveness are taken from non-randomised studies of groups of people where intervention effects are compared with previous or historical information.

Level V. Evidence is from single case studies.

2.3 | Data extraction

One investigator (Layla Edwards) extracted data from included articles into an Excel V15.28 spreadsheet on publication year, country of origin, design, setting, health area, target population, sample size, delirium definition assessment tools, intervention, comparator(s), intervention type (i.e., nonpharmacological or pharmacological), type of economic analysis, perspective (whose costs), time horizon in years (i.e. over what period into the future costs and outcomes were calculated[22]), discount rate, currency, intervention cost, types of costs and outcomes, key results, and sensitivity analyses. The primary investigator (Irina Kinchin) subsequently reviewed the data extraction for all included articles.

The Cochrane-adopted levels of evidence for healthcare interventions[26] were applied to each study (refer to Table A1, Box 1). Both reviewers (Layla Edwards and Irina Kinchin) independently rated each study in three areas: 1. Strength of the evidence; 2. Size of effect; and 3 Relevance of the evidence.[27] Studies were given a rating of I, II, III, IV, or V, with I and II being higher levels of evidence and III, IV and V lower.[27] Investigators compared results and resolved discrepancies through discussion.

Drummond's classification[22] was used to categorise evaluations as full or partial (Figure B1). Full economic evaluations were further classified according to their specific analysis, such as cost-consequences (CCA), cost-effectiveness (CEA), or cost-utility (CUA), and cost–benefit (CBA).[22] CCA examines costs and outcomes without attempting to isolate a single outcome or aggregate outcomes into a single measure. CEA measures outcomes in natural units, such as life-years gained, disability days avoided, or cases detected. In a variant of CEA, called cost-utility analysis, outcomes are measured in terms of preference-based measures of health, such as quality-adjusted life years or disability-adjusted life years. Finally, in CBA, outcomes are valued in monetary units, and results can be expressed as a net return on investment. Two investigators (Irina Kinchin and Dominic Trepel) independently categorised studies as full or

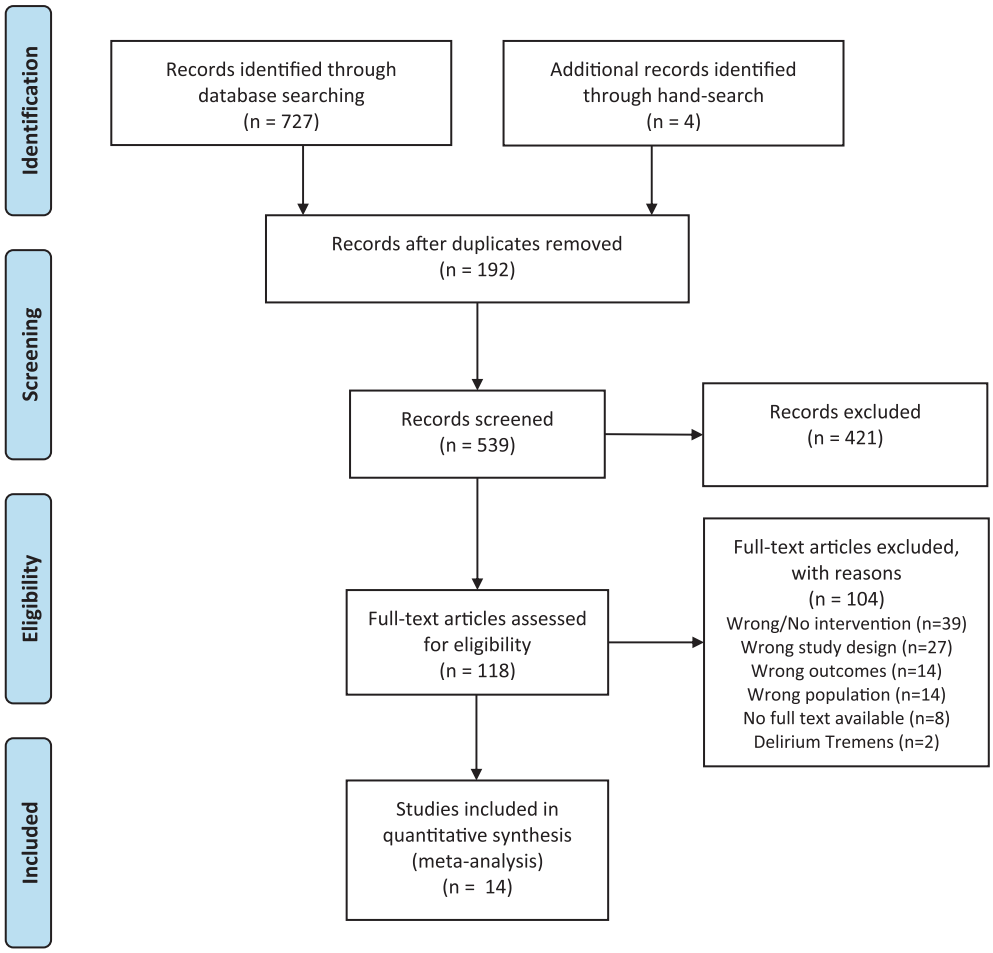

FIGURE 1 PRISMA flow diagram. PRISMA, preferred reporting items for systematic reviews and meta-analyses

partial economic evaluations, compared results, and resolved discrepancies through discussion.

2.4 | Quality assessment

Two investigators (Layla Edwards and Irina Kinchin) evaluated the quality of full economic evaluations using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.[28] Each study scored one point for each criterion that was fully met, half a point if a criterion was 'somewhat' met, and zero for criteria that were either not met ('no') or not applicable. Each paper's quality score was estimated by summing the criteria scores and dividing the total by the number of applicable fields, excluding those that did not apply to a study, and multiplying by 100. The greater the percentage score, the higher the quality of individual studies, according to CHEERS. We also calculated an average percentage score for each CHEERS criterion that was based on the number of 'yes' plus half the number of 'somewhat,' divided by the number of studies for which that criterion was applied. The greater the percentage score, the greater the frequency with which that criterion was met. After the investigators individually assessed studies, they resolved discrepancies in their ratings through discussion.

2.5 | Summary of evidence and adjustment to aid comparison

To allow for international comparison, local currencies in varying years were inflated to the local currency values in 2019, for which the latest statistics were available;[29] and then exchanged to US dollars by using the gross domestic product purchasing power parity (PPP).[30]

3 | RESULTS

The database search resulted in 727 citations, of which 118 had a full-text review. Ten citations met the eligibility criteria, and another four were found through hand-search, resulting in 14 articles for review (Figure 1).

TABLE 1 Included study characteristics

Characteristic	Number (%)	References
Country of origin		
United States	6 (43)	31–36
United Kingdom	3 (21)	37–39
Australia, Finland, Korea, Netherlands, Switzerland	1 each (7)	40–44
Perspective		
United Kingdom NHS and personal social service	3 (21)	37–39
Healthcare system (hospital)	3 (21)	33,35,36
Not reported	8 (57)	31,32,34,40–44
Healthcare setting		
Inpatient	13 (93)	31–34,36–44
Post-discharge follow-up	1 (7)	35
Setting (location)		
General ward	6 (43)	32,34,36,37,39,41
Acute-care ward	1 (7)	37
Surgical Intensive Care Unit (Cardiovascular)	2 (14)	42,44
Medical Intensive Care Unit	1 (7)	31
Surgical ward	1 (7)	38
Community inpatient unit	1 (7)	33
Geriatric ward	1 (7)	40
Post-hospital discharge follow-up (nursing homes and/or community-based inpatient care facility)	1 (7)	35
Not clear	1 (7)	43
Inpatient health area (n = 14)		
General	5 (36)	32–34,36,39
Geriatric	2 (14)	40,41
Medically ventilated	1 (7)	31
Chronic obstructive pulmonary disease	1 (7)	43
Liver transplantation	1 (7)	42
Dementia	1 (7)	37
Hip fracture	1 (7)	38
Cardiovascular	1 (7)	44
Intervention type		
Non-pharmacological	10 (71)	31–37,39,40,43
Both non-pharmacological and pharmacological	4 (29)	38,41,42,44
Intervention name		
Hospital Elder Life Program (HELP)	5 (36)	32–36
Adaptions of HELP	2 (14)	40,43
CareWell in Hospital (CWH)	1 (7)	43
The Recruitment of Volunteers to Improve Vitality in the Elderly (REVIVE)	1 (7)	40
Multi-component delirium prevention	2 (14)	38,39
Standardised delirium management guideline	1 (7)	44
The Awakening and Breathing, Coordination, Delirium monitoring and management, and Early mobilisation (ABCDE) full bundle	1 (7)	31
Delirium prevention strategy	1 (7)	42
Medical and Mental Health Unit (MMHU)	1 (7)	37
Multicomponent geriatric treatment	1 (7)	41
Comparator		
Usual care	12 (86)	32–34,36–44
Breathing trials, Awakening and Delirium monitoring (B-AD) partial bundle	1 (7)	31
Not reported	1 (7)	35
Delirium assessment		
CAM or CAM-ICU	9 (64)	31–33,35,36,38–41
MMSE	6 (43)	35,37–39,41,43
Digit span test	4 (29)	32,35,39,41
Chart review	2 (14)	32,33
DRS-R-98	2 (14)	37
DSM-IV	1 (7)	41
ICD-10	1 (7)	44
ICDSC	1 (7)	44
DSI	1 (7)	38
Assessment of orientation and short-term recall	1 (7)	32
Clinical judgement of a geriatrician	1 (7)	34
Not reported	2 (14)	33,42
Time horizon (years)		
Under 1	2 (14)	40,43
1 to <2	4 (29)	32,37,41,42
2 and over	6 (43)	31,33–36,44
Not reported	2 (14)	38,39
Discount rates (costs and outcomes)		
Costs - 3.5%	2 (14)	38,39
Outcomes - 3.5%	2 (14)	38,39
Not reported	12 (86)	31–37,40–44
Types of costs included		
Inpatient care, incl.	14 (100)	31–44
Length of stay	10 (71)	32–34,36–41,43
Staff allocated time (hours)	7 (50)	32,34,36–38,40,42
Equipment/supplies	5 (36)	32–34,36,42
Medications	5 (36)	31,32,34,41,42

(Continues)

(Continues)

TABLE 1 (Continued)

Characteristic	Number (%)	References
Long term nursing home stay	3 (21)	35,38,39
Hospital maintenance/running cost	2 (14)	33,34
Day-case	2 (14)	37,43
Delirium onset	2 (14)	32,33
New dementia detection	2 (14)	38,39
Adverse events incl. Pressure ulcers and falls	2 (14)	38,39
Intensive care	1 (7)	37
Non-operative care (respiratory support, room and board, laboratory)	1 (7)	31
Consultation costs	1 (7)	42
Visits to specialists	1 (7)	41
Outpatient, incl.	3 (21)	37,41,43
General practitioner visits	2 (14)	37,43
Ambulance service	1 (7)	37
Mental healthcare	1 (7)	37
Social care (housing and meals at home)	1 (7)	37
Home care	1 (7)	43
Day-care	1 (7)	43
Institutionalisation	1 (7)	43
Nursing home service use	1 (7)	41
Patient out-of-pocket, incl.	1 (7)	37
Primary care	1 (7)	37
Types of outcomes		
Delirium occurrence (prevalence/ incidence)	7 (50)	32–34,36,40,42,44
Length of stay	6 (43)	32,33,40,42–44
Mortality	4 (29)	31,35,43,44
Delirium duration	3 (21)	32,40,44
Discharge status	2 (14)	36,40
Quality-adjusted life-years (QALY)	3 (21)	37–39
Delirium severity	2 (14)	40,42
Staff allocation (hours)	2 (14)	40,44
Readmission	2 (14)	40,43
Patient and nurse satisfaction	2 (14)	33,34
Duration of mechanical ventilation	2 (14)	31,44
Adverse events (falls, pressure ulcers, use of restraints)	2 (14)	31,40
Health outcomes (physical and cognitive function)	1 (7)	40
Health-related quality of life (HRQoL)	1 (7)	41
Evidence level		
Model	2 (14)	38,39
Level I	1 (7)	35
Level II	3 (21)	36,37,41
Level III	2 (14)	31,40
Level IV	1 (7)	44
Level V	4 (29)	32–34,43
Unclear	1 (7)	42
Type of economic analysis		
Partial evaluation	8 (57)	31–35,40,43,44
Full evaluation, that is,	6 (43)	36–39,41,42
Cost-utility analysis (CUA) – model-based	2 (14)	38,39
Cost-utility analysis (CUA) – trial-based	1 (7)	37
Cost-consequence analysis (CCA)	2 (14)	36,41
Cost–benefit analysis (CBA)	1 (7)	42

Abbreviations: CAM, confusion assessment method; CAM-ICU, confusion assessment method for ICU patients; CT, computerised tomography scan; DRS-R-98, Delirium rating scale revised-98; DSI, Delirium symptom interview; DSM-IV, diagnostic and statistical manual of mental disorders, (Fourth edition); ICDSC, intensive care Delirium screening checklist; ICD-9-CM, international classification of diseases, ninth revision, clinical modification; ICD-10, international statistical classification of diseases and related health problems, 10th revision; Level I, randomised control trial (RCT), lower limit confidence interval (LL CI) for a measure of effect is above a meaningful benefit in healthcare terms; Level II–RCT, LL CI for a measure of effect is less a meaningful benefit in healthcare terms; but the point estimate still shows effectiveness of the intervention; Level III–non-RCT, concurrent control; Level IV–non-RCT, previous or historical control; Level V–single case study; MDAS, memorial Delirium assessment scale; MMSE, mini–mental state examination; MRI, magnetic resonance imaging; NHS, national health service.

3.1 | Study characteristics

Out of 14 studies, six studies were conducted in the US[31–36] (Table 1; Table C1–C3). The remaining studies came from the United Kingdom (UK) ($n = 3$)[37–39] and one each from Australia,[40] Finland,[41] South Korea,[42] Netherlands,[43] and Switzerland.[44] All studies were published between 2011 and 2020. The mean age range of participants was 50–87 years[31,32,34–36,38–44], excluding two studies that did not report the mean age.[33,37] The majority of evaluations ($n = 13$ out of 14) were conducted in an inpatient (hospital) or ICU setting,[31–34,36–44] and one study was a post-hospital discharge follow-up.[35] Most interventions were non-pharmacological ($n = 10$ out of 14),[31–37,39,40,43] while four (out of 14) incorporated both non-pharmacological and pharmacological components.[38,41,42,44]

Out of 14 studies, six studies (43%) were full economic evaluations.[36–39,41,42] These included three CUA, two model-based[38,39] and one trial based;[37] two CCA[36,41] and one CBA.[42] Only four studies were explicitly termed as economic

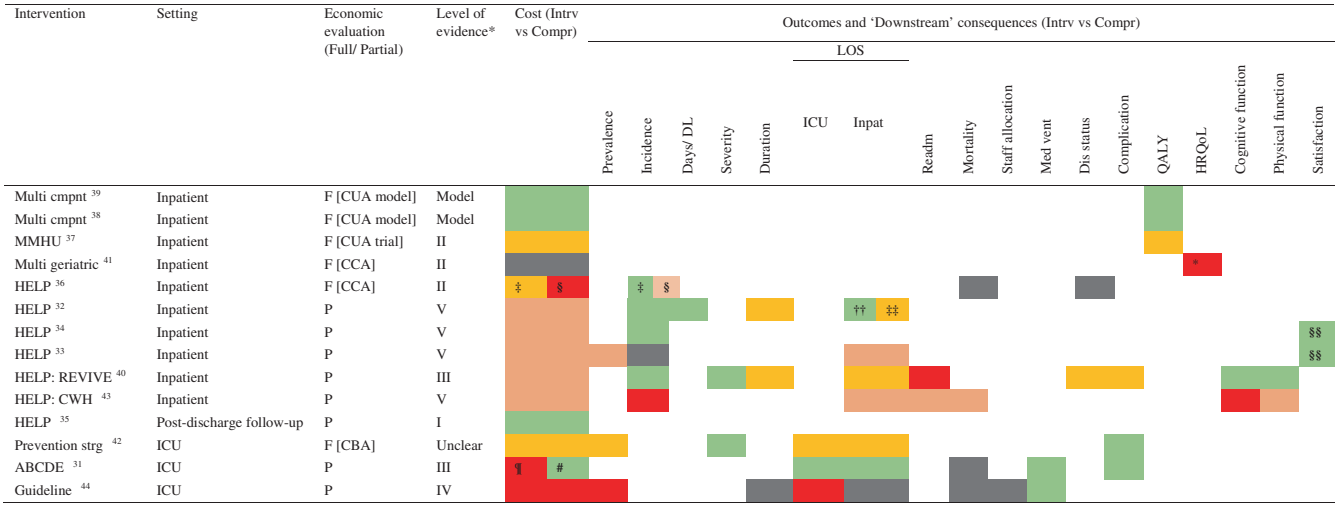

FIGURE 2 Summary of cost and outcomes by intervention. Green – positive change, cost-saving (statistically significant); Orange – positive change, cost-saving (not statistically significant); Pink – statistical significance not reported; Red – negative change (statistically significant); Grey – no statistically significant difference; White – not assessed. *HRQoL deteriorated in both groups as a consequence of delirium. Deterioration was, however, slower in the intervention group (−0.026, 95% CI, −0.051 to −0.001) than in the control group (−0.065, 95% CI, −0.09 to −0.040; $p = 0.034$); ‡ Intermediate risk group; defined as the presence of one risk factor at baseline; § High-risk group; defined as the presence of two to four risk factors at baseline; ¶ Average daily ICU cost; # Total ICU or hospital cost; †† For all and non-delirium patients; ‡‡ For delirium patients; §§ Statistical significance is not applicable, due to satisfaction being measured once. *The Cochrane-adopted levels of evidence. Adapted from AD.Oxman Checklists for review articles. BMJ 1994;309:648–51. Level I. For a randomised controlled trial, the lower limit of the confidence interval (expressed as a range) for a measure of effect is still above a meaningful benefit in healthcare terms; Level II. For a randomised controlled trial, the lower limit of the confidence interval (expressed as a range) for a measure of effect is less than a meaningful beneficial effect in healthcare terms; but the point estimate of effect still shows effectiveness of the intervention; Level III. Measures of effectiveness are taken from non-randomised studies of groups of people where a control group has run concurrently with the group receiving the intervention being assessed; Level IV. Measures of effectiveness are taken from non-randomised studies of groups of people where intervention effects are compared with previous or historical information; Level V. Evidence is from single case studies. ABCDE, Awakening and Breathing, Coordination, Delirium monitoring and management, and Early mobilisation bundle; Cognitive function, measured by the mini-mental state examination (MMSE); Compr, Comparator; CWH, CareWell in Hospital; Complications, ulcers, used of restraints, falls; Days/DL, days with delirium; Dis status, discharge status; DL, delirium; Guideline, Standardised delirium management guideline; EE, economic evaluation; F, full economic evaluation; HELP, Hospital Elder Life Program; HRQoL, Health-related quality of life; Intrv, Intervention; LOS, length of stay; Med vent, medical ventilation; MMHU, Medical and Mental Health Unit; Multi cmpnt, Multicomponent delirium prevention; Multi geriatric, Multicomponent geriatric treatment; P, partial economic evaluation; Physical function, measured by activities of daily living (ADL) scale; Readm, Readmission to hospital; REVIVE, Recruitment of Volunteers to Improve Vitality in the Elderly; Satisfaction, Patient and nurse satisfaction; Staff allocation, Staff allocation (hours) or nursing hours per case; QALY, quality-adjusted life year score.

evaluations.[37–39,42] The remaining eight studies (57%) were partial economic evaluations(Table 1).[31–35,40,43,44]

3.2 | Full economic evaluations

3.2.1 | Multicomponent delirium prevention intervention

Two UK-based studies conducted a model-based cost-utility analysis of a multicomponent delirium prevention intervention among older people undergoing surgical repair of hip fracture[38] and older people admitted to medical wards[39] from a UK NHS and Personal Social Services perspective. The multicomponent delirium intervention was cost-effective compared to usual care in 96.8%[39] and 96.4%[38] of the simulations carried out in the probabilistic sensitivity analysis (Table C1, C2). Costs savings were drawn from the sum of inpatient care, reduced new dementia, reduced length of stay and long-term care, adverse events (falls and pressure ulcers), and staff allocation. The reported annual cost of operating the intervention was $408[39] and $553[38] per patient (all amounts in 2019 US$). CHEERS scores were 77%[38] and 83%[39] accordingly (Figure 3).

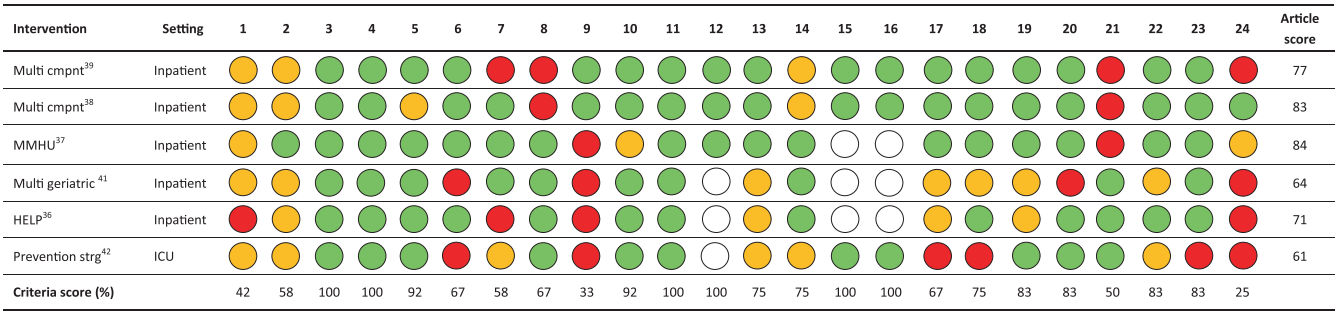

FIGURE 3 CHEERS quality assessment of full economic evaluations. Percentage score is based on the number of 'yes' or met criteria plus half the number of somewhat' or half met criteria, divided by the number of studies for which criteria applied. CHEERS criteria: 1 – Title; 2 – Abstract; 3 – Background and objectives; 4 – Target population; 5 – Setting and location; 6 – Study perspective; 7 – Comparators; 8- Time horizon; 9 – Discount rate; 10 – Choice of outcomes; 11. Measurement of effectiveness; 12 – Measurement and valuation of preference-based outcomes; 13- Estimating resources and cost; 14 – Currency, price date and conversion; 15 – Choice of model; 16 – Assumptions; 17 – Analytical methods; 18 – Study parameters; 19 – Incremental costs and outcomes; 20 – Characterising uncertainty; 21 – Characterising heterogeneity; 22 – Study findings, limitations, generalisability and current knowledge; 23 – Source of funding; 24 – Conflicts of interest. Index: Green – yes; Orange – somewhat; Red – no; White – not applicable. HELP, Hospital Elder Life Program; Multi cmpnt, Multicomponent delirium prevention intervention; Multi geriatric, Multicomponent geriatric treatment; MMHU, Medical and Mental Health Unit; Prevention strg, Delirium prevention strategy.

3.2.2 | Medical and mental health unit

One study examined the cost-effectiveness of the Medical and Mental Health Unit (MMHU) for older people with delirium and dementia admitted to a general hospital from a UK NHS and Personal Social Services perspective using a randomised control trial design.[37] The probability that MMHU was cost-effective ranged between 39% and 94%. This large variation could be attributed to relatively small and not statistically significant changes in the costs and outcomes detected between the intervention and control groups and the methods employed to account for missing data.

The MMHU intervention cost was calculated as the additional staffing costs needed to perform the intervention compared to UC on a general or geriatric ward. The mean per-patient intervention cost was $482. This study was classified as Level II evidence. CHEERS score was 84% (Figure 3).

3.2.3 | Multicomponent geriatric intervention

One study investigated the effect of a multicomponent geriatric intervention on costs of care and health-related quality of life in older people admitted to a general hospital ward using a randomised control trial.[41] The difference in costs between the intervention group and usual care was non-significant. Costs were the sum of all associated inpatient care, including length of stay in various institutions such as hospitals, nursing homes, or long-term care hospitals, visits to specialists, medications and home nursing visits after the index hospitalisation for delirium. Health-related quality of life deteriorated in both groups as a consequence of delirium at discharge and 1-year follow-up. Deterioration was significantly slower in the intervention group compared to the usual care group. Intervention cost was not reported separately. The intervention was reported to reduce health-related quality of life deterioration without increasing the overall cost of care. This study was classified as Level II evidence. CHEERS score was 84% (Figure 3).

3.2.4 | Multicomponent targeted intervention – MTI (adaption of HELP)

A US-based study conducted a longitudinal follow-up from a randomised trial to estimate the incremental cost of long-term nursing home care for patients who received MTI while hospitalised compared to those who did not receive the intervention.[35] The intervention was associated with a cost savings of 15.7% ($p = 0.01$). Costs were calculated by reviewing nursing home use, including length of stay in the one-year follow-up. The cost of the intervention was not reported. This study was classified as Level I evidence. CHEERS score was 71% (Figure 3).

3.2.5 | Delirium prevention strategy

In a Korean surgical ICU, Lee et al evaluated the costs and benefits of the prevention strategy using a clinical record

review.[42] Compared to the usual care, hospitalisation costs among those in the prevention-care group were lower. Costs included inpatient care (consisting of medications, consultation cost, equipment/supplies) and staff allocation (hours). Participants in the prevention-care group had significantly reduced length of stay and complications. Although the prevalence of delirium was reduced for the prevention-care group (35.3% compared to 51.6%) it did not reach significance. The total costs of the prevention strategy were estimated as $32 and included $5 for consultation, $1 for medication, $1 for equipment and $25 for nursing time costs. This study was classified as 'Unclear' evidence. CHEERS score was 61% (Figure 3).

3.3 | Partial economic evaluations

3.3.1 | Hospital elder life program or its adaptation

Six studies evaluated the Hospital Elder Life Program (HELP) program or its adaptation in the inpatient settings using a partial economic evaluation design.[32–34,36,40,43] The annual reported cost of operating HELP ranged between $86,886[32] and $309,172[33] and included personnel and supplies. The corresponding annual financial return of HELP ranged between $1,007,474[32] and $6,204,336.[33] These cost savings were a result of revenue generation acquired from successful delirium prevention (reduced incidence) and reduced length of stay. A study by Rizzo et al.[36] reported per patient cost and financial return of HELP, which were $386 and $532, respectively.

Bakker et al conducted a pilot evaluation of an adaption of HELP called CareWell in Hospital (CWH) in Dutch hospital setting.[43] The intervention demonstrated its feasibility and potential cost savings. In comparison to usual care, CWH resulted in reduced healthcare costs 3 months after discharge. Costs savings were drawn from reduced hospital admissions, visits to a general practitioner, home care, institutionalisation, and day care. Other outcomes, including 'downstream' consequences, were reduction in length of stay, reduction in readmission within 1 month and reduction in death within 3 months post-discharge. The cost of running the CWH was not reported. This study was classified as Level V evidence. CHEERS score was 33% (Figure 3).

Caplan et al evaluated another adaptation of HELP called the Recruitment of Volunteers to Improve Vitality in the Elderly (REVIVE) in the Australian healthcare system.[40] Based on the reduced length of stay and increased use of assistants in nursing, REVIVE showed a total annual saving of $62,978 for the hospital. The cost of REVIVE was not reported. This study was classified as Level III evidence. CHEERS score was 50% (Figure 3).

3.3.2 | Awakening and breathing, coordination, delirium monitoring and management, and early mobilisation bundle

A study from the US measured the impact of the staged implementation of awakening and breathing, coordination, delirium monitoring and management, and early mobilisation (ABCDE) bundle versus breathing trials, awakening and delirium monitoring (B-AD) partial bundle.[31] No cost changes were seen between baseline and partial B-AD bundle, however, there were significant differences between partial B-AD bundle and full ABCDE bundle. Of those, total ICU costs and total hospital costs were reduced. Costs included inpatient, non-operative care (e.g., respiratory support, room and board, laboratory, medications). In addition, the proportion of patients with ICU-acquired pressure ulcers decreased ($p < 0.001$), and the proportion of ICU patient days in restraints decreased ($p < 0.001$) after implementation of Early mobilisation and Coordination in the full bundle (B-AD vs. ABCDE). Furthermore, the duration of medical ventilation was significantly shorter in the full ABCDE bundle compared to partial B-AD bundle, and ICU LOS was significantly shorter across all three periods in the full versus partial bundle ($p < 0.001$). Intervention costs were not reported. This study was classified as Level III evidence. CHEERS score was 71% (Figure 3).

3.3.3 | Standardised delirium management guideline

Schubert et al used a retrospective cohort design with a historical control (pre-intervention) group to test the effectiveness of a standardised multi-professional, multicomponent delirium guideline in a Swiss surgical ICU.[44] Multivariate models comparing the historical usual care group with the intervention group indicated significant increase in delirium period prevalence, the cost per case, length of stay in ICU, and a significant decrease in the duration of mechanical ventilation in the postintervention group. The observed differences in in-hospital mortality, delirium duration, length of stay in the hospital, and nursing hours per case – were not significant. Cost per case was drawn from the sum of individual healthcare costs and overheads per case. Intervention cost was not reported. This study was classified as Level IV evidence. CHEERS score was 69% (Figure 3).

3.4 | Summary of costs and outcomes

Just over half of the evaluations ($n = 8$; 53%) reported the cost of intervention.[32–34,36–39,41,42] Personnel, including additional nursing time, consultation costs, equipment, and medications, were the most included resources. The intervention cost ranged from $386 to $553 per person inpatient and $32 per person in an ICU. HELP implementation cost was reported as between $86,886 and $309,172 per annum.

Three studies and two interventions (multicomponent delirium prevention and HELP) reported significant cost savings or cost offsets somewhere else in the health system (Figure 2).[35,38,39] Two studies observed statistically insignificant changes in cost,[37,42] and two studies[31,36] showed mixed results. Cost savings related to inpatient, outpatient, and out-of-pocket costs ranged between $194–$6022 per person inpatient in general and $4697 per person in ICU. HELP reported cost savings between $62,978 and $6,204,336 per annum.

No intervention demonstrated a positive and statistically significant change in all measured health effects, except for the modelled multicomponent delirium prevention interventions[38,39] and HELP post-discharge follow-up study (Figure 2).[35]

3.5 | Quality assessment

The overall quality of the full economic evaluation studies varied, with CHEERS scores ranging between 61% and 84% (Figure 3). The average score was 74% (± SD 10%). Individual criteria scores ranged from 25% to 100%. The lowest scoring requirements were for declaration of conflicts of interest (criteria 24; score 25%), discount rate (9; 33%), and title (1; 42%).

4 | DISCUSSION

This systematic review examined the economic evidence of interventions for reducing, preventing, and treating delirium. We identified 14 economic evaluations across nine multicomponent and nonpharmacological intervention types aimed mainly at inpatient delirium. Most of the studies (57%) were partial economic evaluations, either because they compared alternatives but focused on costs only (cost analysis), focused on costs only and did not compare alternatives (cost description), or focused on both costs and outcomes but did not compare alternatives (cost-outcome description).

The US HELP program, or its adaptation, was the most evaluated intervention (seven out of 14 evaluations: 50%). HELP is a multicomponent delirium prevention protocol that systematically addresses visual and hearing impairment, immobility, disorientation, sleep deprivation and dehydration.[45] Largely results showed positive financial and health effects associated with HELP. However, the quality of evidence was mostly Level V, meaning that measures of effectiveness came from case studies.

All except for one HELP study[36] were partial economic evaluations. In that study, Rizzo and colleagues[36] showed the differential effect of HELP across groups at varying baseline risk for delirium. HELP significantly reduced healthcare costs among subjects at intermediate risk for developing delirium, but not among high or low-risk subjects. The differential effect of results across groups at varying baseline risk for delirium is an important finding, reinforcing the need to target interventions towards groups most likely to benefit from the intervention strategy.

Similarly, Schubert and colleagues[44] observed mixed results when evaluating multicomponent delirium management guideline implementation in two ICUs. On the one hand, results showed that the implemented guideline led to reduced mechanical ventilation duration independent of multiple disease-associated factors; on the other hand, length of stay in ICU, delirium prevalence and cost per case increased significantly. Based on these results and previous research,[4] economic evaluations of delirium interventions should consider differentiating and targeting patients at varying baseline risks for developing delirium.

All other interventions had limited evidence of mixed results coming from partial economic evaluations, except for the multicomponent delirium prevention intervention, which was evaluated twice via decision-analytic modelling for older people admitted to medical wards[39] and undergoing hip fracture repair.[38] In both instances, the intervention demonstrated cost-effectiveness in the UK healthcare settings in comparison to the usual care.

The largely low-methodological quality of interventions for delirium may stem from several reasons, including the lack of mandatory appraisal. The efficiency of research uptake is being streamlined in pharmaceuticals and medical technologies.[46] Results of a comparative appraisal of these technologies, using explicit cost-effectiveness criteria, are often used to inform resource allocation and enable market access.[46] A comparative cost-effectiveness appraisal of interventions for delirium, using high-standard reporting criteria, would contribute to their improved methodological quality. Every attempt should be made to standardise reporting methods and results, address biases, and deploy explicit and transparent frameworks for incorporating multiple criteria in decision making when value-for-money is uncertain. A full economic evaluation would be recommended over partial evaluation and include a comparison of two or more alternatives and measuring both the immediate costs and

health effects and their 'downstream' consequences (future events averted) as a result of reducing, preventing, or treating delirium.

When appraising interventions for reducing, preventing, or treating delirium, it is essential to standardise outcome measures and account for varying baseline risks for developing delirium and adverse events of clinical importance, such as falls, pressure injuries, malnutrition, and dehydration, with particular attention given to those that differ substantively between the alternatives being compared. Further, the exclusion of certain cost categories might create biases and unexpected consequences when the intervention is implemented. Delirium interventions often employ volunteers to provide nonmedical services, such as providing information, emotional support and reassurance to patients and their families. A societal perspective would be the most pertinent to use when evaluating these interventions. The costs volunteering are often 'hidden,' neither quantified nor explicitly recognised.[47] However, volunteers are not free, and hospitals may incur costs in recruitment, administration, liability, supervision, and recognition.[48] There is no single method for the valuation of volunteer time.[22] From an organisational perspective, volunteer hours' value can be the amount it would cost the organisation to replace volunteers. However, volunteers often undertake more flexible tasks than paid employees with fewer expectations from the organisation and differing productiveness. From the volunteer donor perspective, the opportunity cost of time can be a reasonable measure. This would entail estimates of wages for retired or not in the labour force. Whatever the methodological approach, the study should explicitly acknowledge it by applying the relevant perspective.

Generally, the presentation of all elements of costs and outcomes ought to be in a manner that allows readers to scrutinise the data and methods used and facilitates the transferability of results. Adopting reporting standards, such as, for example, CHEERS statement[28] or Drummond's checklist[22] is highly recommended and would improve the methodological quality of interventions for delirium.

4.1 | Strengths and limitations

There are no previous systematic reviews with a similar scope as ours to the best of our knowledge. While Caplan and colleagues[49] conducted a narrative review of the financial and social costs of delirium and included a summary of interventions, it was not systematic nor assessed the quality of evidence. Although the search strategy aimed at including all studies broadly fitting the pre-set definition of delirium, this review did not include studies characterised by the alternative search term 'acute confusional state,' nor published since June 2020 or non-English literature that may have limited the findings of this review. We took a systematic approach to include only studies where the key concept (delirium) was clearly defined. Despite using a binary system to review and assign quality scores to each study based on the CHEERS adapted checklist, some subjectivity may have biased the scoring. Finally, the studies' heterogeneity prohibited meta-analysis due to the lack of reported standard error/deviation of mean costs and outcomes.

It is worth noting that the cost information is highly context-specific and dependent on the perspective taken and the types of costs included in the analysis. It could vary from country to country and may vary within a country over time. A reader should bear this in mind when making inferences about the cost implications.

To conclude, our findings highlight sparse and generally low-quality economic evidence of delirium interventions in the English language literature. There is insufficient evidence about the factors that determine the cost-effectiveness of delirium reduction efforts, such as models of care, implementation process, or target populations. Directed expansion of health economics towards the evaluation of delirium care is necessary. This will ensure that decisions surrounding the implementation of delirium interventions effectively meet patients' needs and cost-effectiveness if similar outcomes are achieved at less cost or better outcomes for the same cost.

AUTHOR CONTRIBUTIONS

Irina Kinchin conceived and wrote the manuscript. Layla Edwards was involved in data extraction, quality assessment and write up. Dominic Trepel was involved in full and partial economic evaluation classification. Annmarie Hosie and Meera Agar provided critical comments. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. Lorenzoni L, Marinoi, A., Morgani, D., James, C. Health Spending Projections to 2030: New Results Based on a Revised OECD Methodology. France, Paris: OECD;2019.
2. Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. *Nat Rev Neurol*. 2009;5(4):210-220.
3. Koirala B, Hansen BR, Hosie A, et al. Delirium point prevalence studies in inpatient settings: a systematic review and meta-analysis. *J Clin Nurs*. 2020;29(13–14):2083-2092.
4. Wilson JE, Mart MF, Cunningham C, et al. Delirium. *Nat Rev Dis Primers*. 2020;6(1):90.
5. Pisani MA, McNicoll L, Inouye SK. Cognitive impairment in the intensive care unit. *Clin Chest Med*. 2003;24(4):727-737.
6. Haley MN, Casey P, Kane RY, Darzins P, Lawler K. Delirium management: let's get physical? A systematic review and meta-analysis. *Australas J Ageing*. 2019;38(4):231-241.
7. Haggstrom L, Welschinger R, Caplan GA. Functional neuroimaging offers insights into delirium pathophysiology: a systematic review. *Australas J Ageing*. 2017;36(3):186-192.
8. Hamilton GM, Wheeler K, Di Michele J, Lalu MM, McIsaac DI. A systematic review and meta-analysis examining the impact of incident postoperative delirium on mortality. *Anesthesiol: J Am Soc Anesthesiol*. 2017;127(1):78-88.
9. Bellelli G, Moresco R, Panina-Bordignon P, et al. Is delirium the cognitive harbinger of frailty in older adults? A review about the existing evidence. *Front Med*. 2017;4:188.
10. Kinchin I, Mitchell E, Agar M, Trepel D. The economic cost of delirium: a systematic review and quality assessment. *Alzheimers Dement*. 2021;17:1026-1041.
11. Khachaturian AS, Hayden KM, Devlin JW, et al. International drive to illuminate delirium: a developing public health blueprint for action. *Alzheimers Dement*. 2020;16(5):711-725.
12. Lee SY, Fisher J, Wand APF, et al. Developing delirium best practice: a systematic review of education interventions for healthcare professionals working in inpatient settings. *Eur Geriatr Med*. 2020;11(1):1-32.
13. Khan A, Boukrina O, Oh-Park M, Flanagan NA, Singh M, Oldham M. Preventing delirium takes a village: systematic review and meta-analysis of delirium preventive models of care. *J Hosp Med*. 2019;14:E1-E7.
14. Oh ES, Needham DM, Nikooie R, et al. Antipsychotics for preventing delirium in hospitalised adults: a systematic review. *Ann Intern Med*. 2019;171(7):474-484.
15. Nikooie R, Neufeld KJ, Oh ES, et al. Antipsychotics for treating delirium in hospitalised adults: a systematic review. *Ann Intern Med*. 2019;171(7):485-495.
16. Abraha I, Trotta F, Rimland JM, et al. Efficacy of non-pharmacological interventions to prevent and treat delirium in older patients: a systematic overview. The SENATOR project ONTOP series. *PLoS One*. 2015;10(6):e0123090.
17. Siddiqi N, Harrison JK, Clegg A, et al. Interventions for preventing delirium in hospitalised non-ICU patients. *Cochrane Database Syst Rev*. 2016;3:CD005563.
18. Scottish intercollegiate guidelines network (SIGN). Risk reduction and management of delirium: a national clinical guideline. Edinburgh: SIGN;2019.
19. Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med*. 2018;46(9):e825-e873.
20. Hshieh TT, Yang T, Gartaganis SL, Yue J, Inouye SK. Hospital elder life program: systematic review and meta-analysis of effectiveness. *Am J Geriatr Psychiatry*. 2018;26(10):1015-1033.
21. National Institute for Health and Care Excellence (NICE). Delirium: Prevention, Diagnosis and Management. London, UK: NICE;2010.
22. Drummond M, Sculpher M, Claxton K, Stoddart G, Torrance G. *Methods for the economic evaluation of health care programmes*. 4th ed. Oxford; 2015.
23. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8(5):336-341.
24. Schardt C, Adams MB, Owens T, Keitz S, Fontelo P. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak*. 2007;7:16.
25. Jesse S, Bråthen G, Ferrara M, et al. Alcohol withdrawal syndrome: mechanisms, manifestations, and management. *Acta Neurol Scand*. 2017;135(1):4-16.
26. Cochrane and systematic reviews. Levels of evidence for healthcare interventions, 2020.
27. Oxman AD. Checklists for review articles. *BMJ*. 1994;309(6955):648-651.
28. Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS) statement. *J Med Econ*. 2013;16(6):713-719.
29. Consumer Price index. OECD; 2019.
30. Purchasing Power Parities (PPP) Statistics. OECD; 2019.
31. Hsieh SJ, Otusanya O, Gershengorn HB, et al. Staged implementation of awakening and breathing, coordination, delirium monitoring and management, and early mobilization bundle improves patient outcomes and reduces hospital costs. *JAMA Intern Med*. 2019;47(7):885-893.
32. 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):219-226.
33. Rubin FH, Neal K, Fenlon K, Hassan S, Inouye SK. Sustainability and scalability of the hospital elder life program at a community hospital. *J Am Geriatr Soc*. 2011;59(2):359-365.
34. Rubin FH, Williams JT, Lescisin DA, Mook WJ, Hassan S, Inouye SK. Replicating the hospital elder life program in a community hospital and demonstrating effectiveness using

quality improvement methodology. *J Am Geriatr Soc*. 2006; 54(6):969-974.

35. Leslie DL, Zhang Y, Bogardus ST, Holford TR, Leo-Summers LS, Inouye SK. Consequences of preventing delirium in hospitalised older adults on nursing home costs. *J Am Geriatr Soc*. 2005;53(3):405-409.
36. Rizzo JA, Bogardus ST Jr, Leo-Summers L, Williams CS, Acampora D, Inouye SK. Multicomponent targeted intervention to prevent delirium in hospitalised older patients: what is the economic value? *Med Care*. 2001;39(7):740-752.
37. Tanajewski L, Franklin M, Gkountouras G, et al. Economic evaluation of a general hospital unit for older people with delirium and dementia (TEAM randomised controlled trial). *PLoS ONE*. 2015;10(12):e0140662.
38. Akunne A, Davis S, Westby M, Young J. The cost-effectiveness of multicomponent interventions to prevent delirium in older people undergoing surgical repair of hip fracture. *Eur J Orthop Surg Traumatol*. 2014;24(2):187-195.
39. Akunne A, Murthy L, Young J. Cost-effectiveness of multicomponent interventions to prevent delirium in older people admitted to medical wards. *Age Ageing*. 2012;41(3):285-291.
40. Caplan GA, Harper EL. Recruitment of volunteers to improve vitality in the elderly: the REVIVE study. *Intern Med J*. 2007;37:95-100.
41. Pitkala KH, Laurila JV, Strandberg TE, Kautiainen H, Sintonen H, Tilvis RS. Multicomponent geriatric intervention for elderly inpatients with delirium: effects on costs and health-related quality of life. *J Gerontol-Series A Biol Sci Med Sci*. 2008;63(1):56-61.
42. Lee E, Kim J. Cost-benefit analysis of a delirium prevention strategy in the intensive care unit. *Nurs Crit Care*. 2016;21(6): 367-373.
43. Bakker FC, Persoon A, Schoon Y, Olde Rikkert MGM. Hospital elder life program integrated in Dutch hospital care: a pilot. *Am Geriatr Soc*. 2013;61(4):641-668.
44. Schubert M, Bettex D, Steiger P, et al. Implementation of a multiprofessional, multicomponent delirium management guideline in two intensive care units, and its effect on patient outcomes and nurse workload: a pre-post design retrospective cohort study. *Swiss Med Wkly*. 2020;150:w20185.
45. The Center of Excellence for Delirium in Aging: Research T, and Educational Enhancement (CEDARTREE),. Hospital Elder Life Program (HELP) for Prevention of Delirium. 2020; https://www.hospitalelderlifeprogram.org/.
46. National Institute for health and clinical excellence (NICE). Research Recommendations Interim Process and Methods Guide. NICE; 2015.
47. Salamon LM, Sokolowski SW, Haddock MA. Measuring the economic value of volunteer work globally: concepts, estimates, and a roadmap to the future. *Ann Public Coop Econ*. 2011; 82(3):217-252.
48. Handy F, Srinivasan N. Valuing volunteers: an economic evaluation of the net benefits of hospital volunteers. *Nonprofit Voluntary Sector Quarterly*. 2004;33(1):28-54.
49. Caplan GA, Teodorczuk A, Streatfeild J, Agar MR. The financial and social costs of delirium. *Eur Geriatr Med*. 2020;11(1): 105-112.

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APPENDIX A: APPENDICES

TABLE A1 Core concepts and relevant search terms

Delirium	Cost
Delirium or delirium.mp.	"Costs and cost analysis"/or cost.mp
	Economic evaluation or economic evaluation.mp
	Cost-utility analysis/or cost-utility analysis.mp
	Cost–benefit analysis/or cost–benefit analysis.mp
	Cost-minimization analysis/ or cost-minimization analysis.mp
	"Cost of illness" or "cost of illness".mp

APPENDIX B

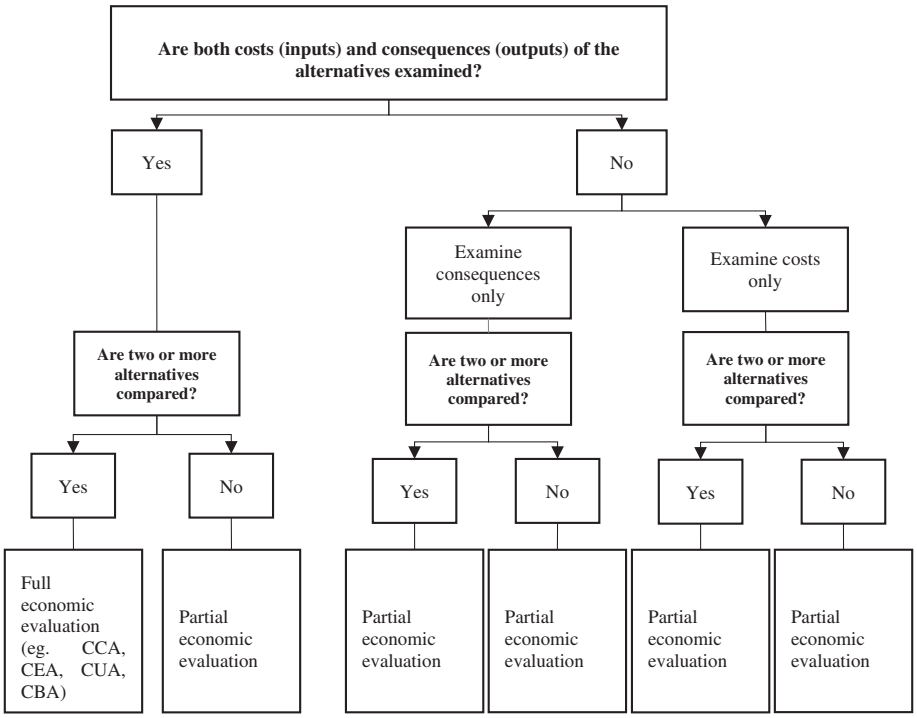

FIGURE B1 Classification scheme for full or partial economic evaluations, adapted from Drummond, Sculpher, Claxton, Stoddart, Torrance.[22] CBA, cost–benefit analysis; CCA, cost-consequences analysis; CEA, cost-effectiveness analysis; CUA, cost-utility analysis

APPENDIX C

TABLE C1 Included studies

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
Schubert, 2020	Switzerland	Retrospective pre-/post-design, cohort study with an historical control (pre-intervention) group	Surgical ICU (Cardiovascular)	≥18 years of age (61.8 ± 14.5)	$N = 3292$ Pre-intervention $n = 1608$; Post-intervention $n = 1684$	Standardised delirium management guideline: Patients in the post-intervention group received standardised multi-professional delirium management which includes four main components: 1. Delirium prevention; 2. Delirium screening; 3. Defined delirium diagnostics; 4. For patients with delirium, defined counter-measures including nonpharmacological and pharmacological interventions	Usual care: patients in the control group received standard care. This included all necessary standard intensive care therapy (e.g., ventilation, pharmacological treatment to stabilise cardiac and/or circulatory disturbances and, if necessary, sedation management), with any non-standardised delirium prevention, diagnosis and treatment in use at that time	2[a]
Hsieh, 2019	US	Prospective cohort study	Medical ICU (mechanical ventilation)	≥18 years of age (At baseline: Partial bundle 64 [54–74] and full bundle 64 [53–75]; Period 1: 66 [53–77] and 64 [51–75], respectively; Period 2: 67 [56–78] and 61 [51–73])	$n = 1855$ Full bundle $n = 1036$ (56%); Partial bundle $n = 819$ (44%)	The awakening and breathing, coordination, delirium monitoring and management, and Early mobilisation (ABCDE) bundle (full bundle): At baseline, spontaneous (B) reathing trials were ongoing in both ICUs; in period 1, (A)wakening and (D)elirium were implemented in both full and partial bundle ICUs; in	B-AD partial bundle: participants received spontaneous (B) reathing trials. and (A)wakening and (D) elirium monitoring/ management	3

(Continues)

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
						period 2, (E)arly mobilisation and structured bundle (C)oordination were implemented in the full bundle (B-AD-EC) but not the partial bundle ICU (B-AD)		
Lee, 2016	Korea	Unclear	Surgical ICU (liver transplantation)	NR (Prevention-care group 50·7 ± 9·1; UC 52·2 ± 8·7)	$N = 130$ Prevention-care group $n = 68$; UC $n = 62$	Delirium prevention strategy: 1. neuropsychiatric consultation, 2. medication according to consultation or patient symptoms, if necessary, 3. avoidance of medication during night (0A-6A), 4. regulation of lighting during night (0A-6A), 5. giving orientation more than three times a day and 6. evaluation of the mental status more than three times a day	Usual care: any participant who did not receive all ($n = 6$) intervention prevention components were assigned to the UC group	1 year and 9 months
Tanajewski, 2015	UK	RCT	Acute geriatric and general medical wards	≥65 years of age (NR)	$N = 600$ MMHU $n = 310$; Standard care $n = 290$	Medical and Mental Health Unit (MMHU): Five areas of enhancement: 1. Additional specialist mental health staff; 2. Staff training in recognition and management of delirium; 3. Organised therapeutic and diversionary activities; 4. The environment was made more appropriate for people with cognitive impairment; 5. A proactive and inclusive approach to family carers was promoted	Usual care: comprehensive geriatric assessment. Staff had general experience in the management of delirium. Mental health support provided on request. None of the MMHU enhancements listed were routine on standard care wards	1 year and 5 months

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
Akunne 2014	UK	Secondary data analysis	Surgical (hip fracture)	Mean starting age used in the model was 79 years	5000 simulations	Multicomponent delirium prevention intervention: comprised an initial proactive consultation (preoperatively); followed by the multicomponent intervention that targeted modifiable risk factors for delirium: orientation, dehydration, sensory impairment, immobility, environmental modifications and medication discontinuation. Patients in the intervention group received targeted recommendations based on a structured protocol from the geriatrician during hospitalisation	Usual care: management by the orthopaedics team on a reactive rather than proactive basis	NR
Bakker, 2013	Netherlands	Pre-/post-design	NR	≥70 years of age (Pre-implementation 78.4 ± 6.3 and CWH 79.0 ± 7.1)	$N = 30$ Pre-implementation $n = 19$; CWH $n = 11$	CareWell in Hospital (CWH): a modified version of the Hospital Elder Life Program (HELP) program. CWH comprises a first-stage screening for risk of delirium, physical decline, falls, and undernutrition by nurses, followed by a second-stage screening by a geriatric nurse, a CareWell plan including a medication review, in-hospital follow-up, and an updated Care-Well plan at discharge. Additional components may include taking a medical history by	Usual care: not described	10 months

(Continues)

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
						proxy; having a geriatrician perform a comprehensive geriatric assessment; discussing a patient in a multidisciplinary meeting; and having trained volunteers perform therapeutic (cognitive) activities, nutritional assistance, or physical activities with patients (mobilisation)		
Zaubler, 2013	US	Pre-/post-design	General	≥70 years of age (Pre-intervention 82.2 ± 7.3; HELP 83.2 ± 6.6)	N = 595 Pre-intervention $n = 215$ (36%); HELP $n = 380$ (64%)	Adapted hospital elder life program (HELP): a multicomponent, delirium prevention protocol targeting six delirium risk factors: cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment, and dehydration. Patients received the intervention from the Elder Life Specialists or volunteers, on weekdays (5 days/week), adapted from the HELP model. The exercise/mobility protocol was omitted due to staffing limitations. Medications likely to cause or exacerbate delirium were flagged and eliminated when possible. In addition, a geriatrician, geriatric nurse practitioner, and/or	Pre-intervention group: outcomes data were recorded on the medical floor (the same unit where interventions subsequently occurred), and patients did not receive any interventions to lower the rate of delirium or decrease length of stay	13 months

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
						psychiatrist would round with the Elder Life Specialists intermittently each week to assess predisposing or modifiable precipitating factors associated with delirium		
Akunne, 2012	UK	Secondary data analysis	Urgent care in a general medical ward	Mean starting age used in the model was 79 years	5000 simulations	Multicomponent delirium prevention intervention: addressed six delirium risk factors: cognitive impairment; sleep deprivation; immobility; visual and hearing impairments and dehydration	Usual care: not described	NR
Rubin, 2011	US	Retrospective pre-/post-study	Community inpatient unit	≥70 years of age (NR)	The program grew from enrolling 940 patients per year on one unit to over 7000 patients per year on 6 units	The HELP model: High fidelity to original HELP model. Adaptations included: the mobility and volume repletion protocols were omitted due to staff shortages during initial months and reinstated when we increased staff. The sleep protocol was modified to include hand rather than back massage. Unit-wide noise reduction strategies were already implemented prior to HELP. Some volunteers were trained by speech therapists in an enhanced feeding protocol. Additionally, some were trained by physical therapists in an enhanced	Usual care: not described	7

(Continues)

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
						mobilisation protocol. The role of our Elder Life Nurse Specialist was modified to omit discharge planning, linkages with community agencies, and post-discharge follow-up with patients, because these functions were already performed by other hospital personnel		
Pitkala, 2008	Finland	RCT	General	≥69 years of age (83)	$N = 174$ Intervention $n = 87$; UC $n = 87$	Multicomponent geriatric treatment: at baseline both groups received a comprehensive geriatric assessment as well as careful diagnosis of the underlying etiological causes of the delirium. Atypical antipsychotics were used if necessary, and effective general treatments were implemented for all patients. After the acute phase of delirium, all patients not recovering from impaired cognition (MMSE <24) in the intervention group underwent detailed diagnostics of dementia and thereafter received acetylcholinesterase inhibitors)	Usual care: a comprehensive geriatric assessment and diagnosis of the underlying etiological conditions at baseline. Atypical antipsychotics and effective general treatments were implemented when necessary	1
Caplan, 2007	Australia	Two controlled before-and-after studies	Geriatric wards	≥70 years of age (REVIVE 85.6 ± 7.4 and UC 83.8 ± 4.7)	Study 1 (program effectiveness) $N = 37$	Volunteers to improve vitality in the Elderly (REVIVE): based on HELP: The intervention was led by	Usual care: not described	10 months

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
					UC $n = 21$; REVIVE $n = 16$	volunteers. The five intervention strategies implemented on the wards from 14 to 19 h each weekday were: 1. Reorientation through writing and talking; 2. Therapeutic activities that involved cognitive stimulation; 3. Feeding assistance; 4. Hydration assistance to prevent or treat dehydration. 5. Vision and hearing protocols. Special communication aids were provided if needed		
Rubin, 2006	US	Pre-/post-test quality-improvement study	General	≥70 years of age (Pre-intervention 80.6 ± 6.2 and HELP 80.9 ± 6.7)	$N = 1929$ (patients with delirium). Pre-intervention $n = 1225$; HELP $n = 704$	HELP: Three main volunteer intervention deviations occurred from the original HELP model: 1. Exercise and fluid repletion protocols were omitted due to insufficient staff; 2. the sleep protocol was modified to include partial sleep-enhancement activities; 3. a nurse practitioner evaluated patients for delirium and for modifiable predisposing or precipitating factors	Usual care: a proxy measure of delirium was developed using administrative data to calculate delirium rate and differences in variable costs of care and length of stay for patients before the intervention	2[b]
Leslie, 2005	US	Longitudinal follow-up from an RCT	Post-hospital discharge settings: nursing homes and/or community based inpatient care facilities	≥70 years of age (HELP 81.5 ± 6.9; Control 81.9 ± 6.6)	$n = 801$ HELP $n = 400$; Control $n = 401$	Multicomponent targeted intervention (MTI) called HELP: consisted of interventions targeting six delirium risk factors: cognitive impairment, sleep deprivation, immobility,	Control group: participants who did not receive the intervention	3

(Continues)

TABLE C1 (Continued)

Author, year	Country	Study design	Setting	Target population (mean age ± SD or range)	Sample size	Intervention	Comparator(s)	Time horizon (years)
						vision impairment, hearing impairment, and dehydration		
Rizzo, 2001	US	RCT	General ward	≥70 years of age (HELP 79.64 ± 6.09; UC 79.80 ± 6.23)	N = 852 HELP $n = 426$; UC $n = 426$	MTI called HELP: consisted of strategies targeting six delirium risk factors: cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment, and dehydration. Core strategies included: orienting communication, therapeutic activities, sleep enhancement strategies, exercise and mobilisation, provision of vision and hearing aids, and oral volume repletion for dehydration. Other strategies included geriatric nursing assessment and interdisciplinary rounds	Usual care: not described	3

Abbreviations: CA, cost analysis; CBA, cost benefit analysis; CHEERS, xxx; CUA, cost utility analysis; EE, economic evaluation; F, full economic evaluation; ICU, intensive care unit; MMSE, mini-mental state examination; N, no; NHS, national health service; Non-pharma, non-pharmacological intervention; NR, not reported; P, partial economic evaluation; Pharma, pharmacological intervention; PSS, personal social services; RCT, randomised control trial; UC, usual care; UK, United Kingdom; US, United States; Y, Yes.

[a]Pre-intervention was a historical group between Jan-Dec 2011 and then post intervention was Jan–Dec 2013.

[b]Baseline (pre-intervention) data were measured throughout 2001, and phase in data were collected from January 1 through June 30, 2002. Between July 1 and December 31, 2002, the HELP team assessed all patients aged 70 and older.

TABLE C2 Study results

Author, year	Interventions compared	Discount rate; currency (price date)	Intervention cost	Types of costs	Main source of data	Results: Change in (all values as reported in studies)		ICER	Deterministic sensitivity analyses	Probability of being cost-effective[a]
						Cost	Outcome			
Schubert, 2020	Standardised delirium management guideline versus UC	NR; CHF (2011 and 2013)	NR	Inpatient care (sum of all individual healthcare costs and overheads per case)	Minimal data set ICU; Swiss Federal Statistical Office data set; ICDSC Assessment data; Care Performance and Process Documentation (Leistungserfassung in der Pflege)	Total cost per case increased from CHF 49,440 (range 47.4–51.5) in 2011 to CHF 55,940 (range 54.0–57.9) in 2013	*LOS in ICU and hospital*: In 2011 patients stayed roughly 2.5 days (2.4–2.6) compared to 2.6 days (2.5–2.7) in 2013. Overall stays were 17.1 days (in 2011) and 18.1 days (in 2013) in the hospital. *In-hospital mortality*: In 2011, 84 (5.2%) and in 2013, 96 (5.4%) patients died during their hospital stay[b] *Prevalence of delirium*: 200 (12%) in the control group and 334 (21%) in the post-intervention group received a delirium diagnosis based on their ICD-10 code. Based on the ICDSC scores ≥4, 816 patients, 214 in the control group and 602 in the post-intervention group patients, were diagnosed as delirious. *Delirium duration*: $n = 572$ ICU patients identified as delirious (ICDSC ≥4) spent a mean of 3 days (3.6 in 2013, 3.3 in 2011) delirious. *Duration of mechanical ventilation*: In both years, patients spent on average just under one day (2011: 23.8 h, 2013: 23.6 h) on mechanical ventilation. *Nursing workload*: In 2011, nurses spent on average roughly 26 h and in 2013, 28.5 h per case on direct patient care.	NA	NR	NR
Hsieh, 2019	The ABCDE full bundle versus B-AD partial bundle	NR; $NR (2012–2013)	NR	Inpatient, non-operative care (e.g., respiratory support, room and board, laboratory, medications)	Clinical data were extracted from electronic medical records using healthcare surveillance software. Costs were determined using cost-to-charge ratios at Montefiore Medical Center. Clinical quality metrics were obtained from aggregate hospital-reported data for Centers for Medicare and Medicaid Services quality indicators.	Cost outcomes: Baseline versus Period 1% Change (95% CI) (B minus B-AD)–Average daily ICU cost 2.69 (−4.9–10.9; $p = 0.50$); Total ICU cost −0.47 (−22.3 to 27.4; $p = 0.97$); Total hospital cost −0.06 (−21.4 to 27.0; $p = 0.10$). Period 1 versus Period 2% Change (95% CI) (B-AD minus B-AD-EC) –average daily ICU cost 4.4 (−4.5 to 14.1; $p = 0.34$); Total ICU cost −24.2 (−41.4–−2.0; $p = 0.03$); total hospital cost −30.2 (−46.1–−9.5; $p = 0.007$)	*Clinical Quality Outcomes*: The proportion of patients with ICU-acquired pressure ulcers decreased (39% to 23%; $p < 0.001$) and the proportion of ICU patient days in restraints decreased (30% to 26%; $p < 0.001$) after implementation of EC in the full bundle ICU (period 1 vs. 2). In contrast, the prevalence of ICU-acquired pressure ulcers increased (18% to 23% of patients; $p = 0.04$) and proportion of ICU days in restraints increased (50% to 54%; $p = 0.001$) in the partial bundle ICU during the same period. *Clinical Outcomes*: The duration of mechanical ventilation was significantly shorter in period 2 in the full versus partial bundle ICU, and ICU LOS was significantly shorter across all three periods in the full versus partial bundle ICU ($p < 0.001$). Hospital LOS and hospital mortality did not differ across all periods in both ICUs.	NA	NR	NR

(Continues)

TABLE C2 (Continued)

Author, year	Interventions compared	Discount rate; currency (price date)	Intervention cost	Types of costs	Main source of data	Results: Change in (all values as reported in studies)		ICER	Deterministic sensitivity analyses	Probability of being cost-effective[a]
						Cost	Outcome			
Lee, 2016	Delirium prevention strategy versus UC	NR; $NR (2007–2008)	The total costs of the prevention strategy were $38·4, including $5·8 for consultation, $1·7 for medication, $0·8 for equipment and $30·1 for nursing time costs.	Inpatient care, incl. Medications, consultation cost, equipment/supplies, staff allocation (hours)	Review of relevant medical records	Hospitalisation costs were estimated as $26,181 in the prevention-care group and $31,759 in the UC group	*Delirium*: Less participants in the prevention-care group (35.3%) experienced an episode of delirium compared to the UC group (51.6%), however this did not reach significance ($p = 0.061$) *Complication*: those who had an episode of delirium were divided into a complication group and non-complication group. Less prevention-care participants were not classified as a complication (85.3%) compared to UC participants (69.4%) ($p = 0.029$). *APACHE II score at transfer*: prevention care group had a mean score of $8{\cdot}0 \pm 3{\cdot}9$ compared to mean score $11{\cdot}3 \pm 8{\cdot}4$ for UC ($p = 0{\cdot}006$) *LOS*: mean LOS for prevention care group was 7.3 ± 3.8 days compared to 9.6 ± 8.9 days in the UC group ($p = 0.057$)	NA	The net benefit $2103.5–$9153.7 by prevalence rate and $4660.8–$5715.0 by complication rate in both groups. The benefit cost ratio was from 55.8 to 239.4 by prevalence rate and from 122.4 to 149.8 by complication rate	NR
Tanajewski, 2015	MMHU versus UC	NR; £Pound (2011–2012)	Mean per-patient intervention cost £368 (95% CI: 334, 410)	Inpatient care, incl. Staff allocation (hours), LOS, day-case, intensive care. Outpatient care, Incl. General practitioner, ambulance services, and mental healthcare. Social care, incl. Home, residential and telecare, housing and meals at home services. Patient costs incl. Primary care.	Hospital's medical admissions log	The total adjusted health and social care costs, including direct costs of the intervention, at 3 months was £7714 and £7862 for MMHU and standard care groups (difference -£149 (95% CI: −298, 4)	The difference in adjusted QALYs gained was 0.001 (95% CI: −0.006, 0.008)	58% probability of the MMHU being dominant (cost-saving with QALY benefit)	NR	At £20,000/QALY threshold, the probability of cost-effectiveness was 94%
Akunne, 2014	Multicomponent delirium prevention intervention versus UC	3.5%; £Pound (NR)	£511 (SE = £65) per person	Inpatient care, cost of new dementia, long-term care, LOS, cost of adverse events (falls, pressure ulcer), staff allocation (hours)	Marcantonio ER, Flacker JM, Wright RJ, Resnick NM (2001) Reducing delirium after hip fracture: a randomised trial. J Am Geriatr Soc; 49(5): 516–522	Mean cost: £19,530 UC, £17,040 multicomponent delirium prevention intervention; incremental cost --£2490	Mean QALYs 1.54 UC and 1.82 multicomponent delirium prevention intervention; incremental QALYs 0.29	Multicomponent intervention dominated UC	INMB (base case) of £8070. The lowest INMB: -£62 (Extended hospital stay is the only consequence of delirium). The highest INMB: £8760 (Life expectancy for dementia patients with previous delirium)	INMB £8180; intervention was cost-effective in 96.4% of the simulations
Bakker, 2013	CWH (HELP adaption) versus UC	NR; €Euro (NR)	NR	Inpatient care, incl. Hospital admission, LOS, additional healthcare resources, incl.	Electronic medical files	The mean cumulative costs per patient 3 months after discharge were €11,240 for controls and	*LOS*: means days before implementation 11.1 ± 8.2 compared to after implementation 10.0 ± 8.6	NA	NR	NR

TABLE C2 (Continued)

Author, year	Interventions compared	Discount rate; currency (price date)	Intervention cost	Types of costs	Main source of data	Results: Change in (all values as reported in studies)		ICER	Deterministic sensitivity analyses	Probability of being cost-effective[a]
						Cost	Outcome			
				Visits to a general practitioner, home care, institutionalisation, and day care.		€9133 for the intervention group	*Readmission within 1 month in this hospital*: before implementation 25% of patients returned to hospital compared to 7.1% after implementation *Died within 3 months after discharge*: 17.9% of participants in the pre-implementation group died 3-months after discharge as opposed to 14.3% after implementation			
Zaubler, 2013	HELP versus pre-intervention group	NR; $NR (NR)	NR	Inpatient care, incl. Staff allocation (hours), medications and supplies, cost of delirium onset, and LOS	MISSING	Cost savings and potential increased revenues associated with patients enrolled in the intervention group: $1,122,000 annually	*Delirium*: The episodes of delirium decreased from 20% of the pre-intervention group to 12% of the intervention group, with a significant relative 40% reduction ($p = 0.019$) *Patient-days with delirium*: Total patient-days with delirium decreased from 129 (8%) in the pre-intervention group to 123 (6%) in the intervention group ($p = 0.005$) *Delirium duration* = The duration of delirium episodes decreased from a median of 2.5 days in the pre-intervention group to a median of 2 days in the intervention group ($p = 0.22$) *LOS*: the median LOS among all patients significantly decreased from 6 days to 4 days ($p = 0.001$). Among delirious patients (n = 89), median LOS in the pre-intervention group was 7 days versus 5 days in the intervention group ($p = 0.18$). Among non-delirious patients (n = 506), median LOS in the pre-intervention group was 5 days versus 4 days in the intervention group ($p = 0.001$)	NA	NR	NR
Akunne, 2012	Multicomponent delirium prevention intervention versus UC	3.5%; NR; £Pound (NR)	£377 (SE = £48) per person	Inpatient care, cost of new dementia, long-term care, LOS, cost of adverse events (falls, pressure ulcer), staff allocation (hours)	Inouye SK, Bogardus ST Jr, Charpentier PA et al. (1999) A multicomponent intervention to prevent delirium in hospitalised older patients. N Eng J Med; 340: 669–76	Mean cost: UC £13,200 and multicomponent intervention £12,690; incremental cost −£520	Mean QALYs UC 2.140 and multicomponent intervention 2.220; incremental QALYs 0.084	Multicomponent intervention dominated UC	INMB (base case) of £2130. The lowest INMB -£370 (Pressure ulcer is the only consequence of delirium). The highest INMB: £2330 (Life expectancy for dementia	INMB of £2200; intervention was cost-effective in 96.8% of the simulations

(Continues)

TABLE C2 (Continued)

Author, year	Interventions compared	Discount rate; currency (price date)	Intervention cost	Types of costs	Main source of data	Results: Change in (all values as reported in studies)		ICER	Deterministic sensitivity analyses	Probability of being cost-effective[a]
						Cost	Outcome			
							patients with previous delirium)			
Rubin, 2011	HELP versus UC	NR; US$ (2008)	The costs of operating the HELP program in the first year was $127,000. In 2008, the costs of the expanded program, incl. Personnel and supplies, were $439,440	Inpatient care, delirium onset, LOS, hospital costs, and program supplies (therapeutic activities equipment, hearing and vision adaptation equipment, large-print magazines, office supplies, and recruitment costs for volunteer)	Hospital administrative database	Total cost saving (reduction in variable cost X delirium cases prevented/year) $2,031,440. Total revenue generated (from delirium prevention plus reduction in LOS) $5, 337, 109. Financial return from HELP per year $7,368,549	*Delirium*: the baseline delirium rate was 41% prior to HELP in 2001. In 2002, the rate was 26%, a decrease of 15% compared to baseline. In 2008, the rate was 18% based on direct observation, a decrease of 23% compared to baseline. Notably, incident delirium—that is, delirium of new onset during hospitalisation, remained at 3% or less from 2004–2008 *Patient and nurse satisfaction*: Patients reported being highly satisfied with their care on the HELP program. Nurses reported benefit and satisfaction with the HELP program, agreeing with the statement that their job was "more satisfying due to HELP" *LOS*: In delirious patients on the HELP program, LOS reduced by 1.0 day in 2002, and by 2.8 days in 2008, relative to delirious patients not receiving HELP at baseline. For patients enrolled in HELP who were not delirious, LOS was reduced by 0.1 days in 2002 and 0.8 days in 2008, compared to non-delirious patients not receiving HELP at baseline	NA	NR	NR
Pitkala, 2008	Multicomponent geriatric treatment versus UC	NR; €Euro (2007)	NR	Inpatient care, incl. LOS in various institutions (hospitals, nursing home, or long-term care hospitals), and visits to specialists; medications and home nursing visits.	Patients' medical records and proxy interview	Counting all costs of care, the intervention group used a mean 19,737 € per patient during the follow-up year, whereas the respective figure for the control group was 19,557 €. The difference between the groups was not significant (180 €, 95% CI, −5006 to 5064 €). The total cost for the whole intervention group was 1,722,763 €, and the total cost for the control group was 1,702,258 €	*Dementia*: 31% had prior dementia, 26% intervention 35% control ($p = 0.25$) *HRQoL*: HRQoL was significantly higher in the intervention than in the control group (0.68 ± 0.12 versus 0.62 ± 0.15; $p = 0.020$). HRQoL deteriorated in both groups as a consequence of delirium, deterioration was slower in the intervention (−0.026, 95% CI, −0.051 to −0.001) than in the control group (−0.065, 95% CI, −0.09 to −0.040). Among those patients having both HRQoL assessments available, the median time between the baseline assessment and the discharge assessment was 18 days in the intervention group (n = 79) and 16 days in the control group (n = 77) ($p = 0.58$)	NA	NR	NR
Caplan, 2007	REVIVE (HELP adaption) versus UC care	NR; $AU (NR)	Total cost of project at 4 months (before) $22,961 and at 12	Inpatient care, incl. LOS and staff allocation (hours)	Data were collected non-blinded by the geriatric registrar and volunteer coordinator	Study 1: Based on reduced length of stay, the benefit of REVIVE over 12	*Health outcomes*: Volunteer-assisted patients showed a lower incidence of delirium	NA	NR	NR

TABLE C2 (Continued)

Author, year	Interventions compared	Discount rate; currency (price date)	Intervention cost	Types of costs	Main source of data	Results: Change in (all values as reported in studies)		ICER	Deterministic sensitivity analyses	Probability of being cost-effective[a]
						Cost	Outcome			
			months (after) $68,883			months $123,840. The theoretical amount saved because of decreased LOS over a 12-month period: $123,840 - $68,883 = $54,957. Study 2: mean monthly AIN hours were 330 versus 644 h. This gave a total saved time of 314 h/month. At an hourly rate of $19.70, this is a saving of $6185/month or over $74,229 per year. Combining the two areas suggests that a total annual saving of A $129,186 for the hospital from REVIVE	(intervention 6.3% vs. control 38.1%; $p = 0.032$) and a reduction in the severity of delirium (mean MDAS 1.2 vs. 5.1, respectively; $p = 0.045$). A clinical trend was seen towards a reduction in the duration of delirium (5.0 days vs. 12.5 days; $p = 0.64$) incidence of falls (6.3 vs. 19.0%; $p = 0.26$) and residential aged care placement (25.0 vs. 47.6%; $p = 0.16$). However, there was also a trend towards increased unplanned readmissions at 1 month for the intervention group (31.3 vs. 19.0%; $p = 0.39$). Patients enrolled in REVIVE had better improvement in cognitive (MMSE change +3.6 vs. 20.6; $p = 0.019$) and physical function, compared with baseline (ADL scores 22.0 vs. 25.29; $p = 0.049$). Furthermore, there was a statistical trend towards reduction of LOS from enrolment in the intervention group by 4.3 days ($p = 0.35$) *Monthly AIN hours*: mean monthly AIN hours were 330 (before) versus 644 h (after)			
Rubin, 2006	HELP versus UC	NR; $NR (NR)	The variable cost per case of a delirious patient was $4995, whereas a non-delirious patient cost only $2814	Inpatient care, incl. Medications, supplies, staff allocation (hours), LOS and hospital maintenance (payment of debt service, building maintenance, and compensation for nonclinical employees).	Direct observations by geriatricians and NPs	Each patient who was prevented from becoming delirious therefore saved the hospital $2181. Thus, for 101 cases prevented, the cost savings amounts to $220,281. Preventing 101 cases equals 364 bed-days saved, allowing the hospital to admit additional patients to those beds. During this 6-month period, each bed generated $170,000, for an additional $340,000 cost savings. During full implementation, total LOS for patients who developed delirium decreased by 0.3 days (P5.32). The costs associated with treating delirious patients also decreased $790 (P5.46) per patient from baseline, for a total savings of $48,980. Altogether, the cost savings of this program amounted to $626,261	*Delirium rate*: Delirium rates for the baseline, phase-in, and intervention periods decreased from 40.8% ($n = 5166$) to 33.0% ($n = 589$) to 26.4% ($n = 562$), respectively. The difference from baseline to intervention was significant ($p = 0.002$). The relative delirium reduction was 35.3%. The delirium rates continued to be lower than baseline in 2003 (34.3%, $n = 5156$; $p = 0.12$) and in the first half of 2004 (32.3%, $n = 571$; $p = 0.09$), 1 and 2 years, respectively, after HELP was implemented *Nursing and Patient Satisfaction*: Nurses and nurses' aides found benefit and satisfaction from the implementation of the program. On a 5-point scale, 5 being the highest agreement, nurses and nurses' aides agreed (3.8 and 4.3, respectively) with "My job is more satisfying due to HELP." They also highly agreed (4.8 for both) with the item "It would be helpful to make HELP a permanent program on my unit." Patients were also satisfied with the HELP	NA	NR	NR

(Continues)

TABLE C2 (Continued)

Author, year	Interventions compared	Discount rate; currency (price date)	Intervention cost	Types of costs	Main source of data	Results: Change in (all values as reported in studies)		ICER	Deterministic sensitivity analyses	Probability of being cost-effective[a]
						Cost	Outcome			
						over 6 months. The overall cost of HELP, including personnel and supplies, was $63,650, for a net cost savings of an estimated $562,611 in 6 months on one 40-bed nursing unit	program, rating it 2.8 out of 3.0 for overall satisfaction			
Leslie, 2005	HELP versus control group	NR; $NR (NR)	NR	Inpatient care, incl. Long-term nursing home stay.	Primary data collected during the RCT	Total costs per patient: Intervention $50,881, Control $60,327, difference − 9446	*One year follow-up period*: 38% ($n = 153$) of HELP versus 37% ($n = 148$) control group participants had any nursing home stay. Of those, 51 (13.5%) and 54 (12.7%), respectively, were long-term nursing home patients. Death during follow-up were 97 (24%) compared to 89 (22%)	NA	NR	NR
Rizzo, 2001	HELP versus UC	NR; US$ (1999)	Total intervention costs were $257,385 across the 3-year study period	Inpatient care, incl. Staff allocation (hours) and LOS. Equipment and supplies (overhead expenses e.g. computer supplies, telephone, pager rentals, photocopying, batteries, office supplies; and supplies needed for each intervention protocol	Clinical researchers based on direct observations	Total cost savings, excluding HELP costs, was $831 for the intermediate-risk group receiving the HELP strategy as compared with UC ($p = <0.05$); The high-risk group receiving the HELP increased overall costs of $426, however it did not reach significance. Total cost saving, including the HELP costs, was $99 for the intermediate-risk group, however this did not reach significance; The high-risk group increased costs to $1308 ($p = <0.05$)	*Delirium incidence*: the intermediate risk cohort receiving the HELP had a 6.5% incidence of delirium, compared with 11.7% in UC ($p = <0.05$). Among the high risk cohort, the corresponding incidence of delirium was 19% compared to 24%, respectively. Overall incidence of delirium (intermediate and high risk combined) was 9.9% compared to 15% ($p = <0.05$) *Discharge status*: patients in the intervention and UC groups did not differ significantly – death (1% vs. 2%), nursing home (23% vs. 20%), home or independent living (71% vs. 74%), and other (5% vs. 4%)	NA	Estimated cost savings vary from $415 to $1689 in the intermediate risk cohort	NR

Abbreviations: AIN, assistants in nursing; APACHE II, acute physiology, age, and chronic health evaluation II; CHF, Swiss Franc; CT, computerised tomography scan; EEG, electroencephalograms; HELP, hospital elder life program; HRQoL, health-related quality of life; ICDSC, intensive care delirium screening checklist; ICER, incremental cost-effectiveness ratio; INMB, incremental net monetary; benefit; LOS, length of stay; LP, lumbar puncture; MRI, magnetic resonance imaging; NA, not applicable; NR, not reported; QALY, quality-adjusted life year; REVIVE, recruitment of volunteers to improve vitality in the elderly; UC, usual care; $NR, dollar currency not reported; US$, US dollar.

[a]Probabilistic sensitivity analyses.

[b]Authors reported conflicting in-hospital figures, with the in-text and table figures not matching. For our extraction we used the table results.

TABLE C3 Delirium assessment tools

Study	Setting	Health area	Main data source	Definition of delirium
Schubert, 2020	Hospital	ICU surgical (cardio)	Minimal Data Set ICU, ICDSC Assessment data, Care Performance and Process Documentation	ICD-10 delirium diagnosis (F050, F051, F058, F059, F104) and additionally (in the post-intervention group) on one or more ICDSC assessment scores (ICDSC ≥4)
Lee, 2016	Hospital	ICU surgical (liver transplantation)	Relevant medical records	ICD-9-CM delirium codes: drug-induced delirium (292.81), vascular dementia with delirium (290.41), presenile dementia with delirium (290.11), senile dementia with delirium (290.3), delirium due to conditions classified elsewhere (293.0), altered mental status (780.97), transient mental disorders due to conditions classified elsewhere (293) and subacute delirium (293.1)
Hsieh, 2019	Hospital	ICU medical	Clinical data were extracted from electronic medical records using healthcare surveillance software	Twice daily delirium assessments using the CAM-ICU by nurses
Akunne, 2012	Hospital	Urgent care and general medical ward	Inouye SK, Bogardus ST Jr, Charpentier PA et al. (1999) A multicomponent intervention to prevent delirium in hospitalised older patients. N Eng J Med; 340: 669–76	NR. This was a modelling study that draw evidence on the clinical effectiveness of multicomponent interventions for delirium prevention from a randomised trial. In the trial the screening interview included the MMSE, the Digit Span Test, evaluation by CAM, assessment of Katz's Activities of Daily Living, the standard Jaeger test for vision, and chart review to determine APACHE II score
Zaubler, 2013	Hospital	General	Medical record	CAM assessed by the Elder Life Specialists. A brief cognitive screen that included assessment of orientation, short-term recall, and the Digit Span Test was used as the basis to score the CAM and to assess for the presence of cognitive impairment in patients. Delirium was noted as a binary outcome (present or absent) based on either a positive CAM or, on weekend days and holidays when a CAM assessment could not be completed, delirium was assessed by reviewing the medical record and noted as present when there was documentation of an acute mental status change consistent with delirium.
Pitkala, 2008	Hospital	General	Patients' medical records and proxy interview	Patients were screened within 2 working days of their admission by administration of the CAM test, MMSE, and Digit span. Among participants with a positive CAM test, delirium was further confirmed by the DSM-IV

(Continues)

TABLE C3 (Continued)

Study	Setting	Health area	Main data source	Definition of delirium
Rizzo, 2001	Hospital	General	Clinical researchers based on direct observations	Defined according to the CAM criteria
Tanajewski, 2015	Hospital	Acute geriatric and general medical wards	Hospital's medical admissions unit	Delirium at admission (measure by DRS-R-98, >18/46) and severe cognitive impairment (measured by MMSE, < 9)
Caplan, 2007	Hospital	Geriatric wards	Data were collected non-blinded by the geriatric registrar and volunteer coordinator	Patients were assessed for delirium every second weekday by the registrar using the CAM. If positive, the MDAS was used to assess severity of delirium.
Akunne, 2014	Hospital	Surgical (hip fracture)	Marcantonio ER, Flacker JM, Wright RJ, Resnick NM (2001) Reducing delirium after hip fracture: a randomised trial. J Am Geriatr Soc; 49(5): 516–522	NR. This was a modelling study that draw evidence on the clinical effectiveness of multicomponent interventions for delirium prevention from a randomised trial. In the trial delirium was assessed using the CAM diagnostic algorithm complimented with the MMSE, DSI, and MDAS tools.
Bakker, 2013	Hospital	NR	Data were collected by a geriatrician	Clinical judgement of a geriatrician
Rubin, 2011	Hospital	Community inpatient unit	Hospital administrative database	Delirium was determined by the Elder Life Nurse Specialist during a direct bedside assessment using the CAM
Rubin, 2006	Hospital	Nursing unit	Direct observations by geriatricians and NPs	A proxy measure for delirium was devised to identify all patients in the usual care group who were charged for a restraint device or for one of the major tranquilisers most commonly used for the treatment of acute agitation in hospitalised older people in the community (haloperidol, risperidone, or quetiapine). A NP evaluated patients in the HELP group for the presence of delirium and for the presence of modifiable predisposing or precipitating factors. Delirium assessment tool was not reported.
Leslie, 2005	Outpatient	Post-hospital discharge settings: nursing Homes and/or community based inpatient care facilities	Primary data collected during the RCT	NR. The study provided a reference to the initial trial that used the following screening mechanism: the MMSE, the Digit Span Test, evaluation by CAM, assessment of Katz's Activities of Daily Living, the standard Jaeger test for vision, and chart review to determine the APACHE II score

Abbreviations: APACHE II, acute physiology, age, and chronic health evaluation II; CAM, the confusion assessment method; CAM-ICU, the confusion assessment method for ICU patients; DRS-R-98, Delirium Rating Scale Revised-98; DSI, delirium symptom interview; DSM-IV, diagnostic and statistical manual of mental disorders, fourth edition; ICDSC, intensive care delirium screening checklist; ICD-9-CM, the international classification of diseases, ninth revision, clinical modification; ICD-10, the international statistical classification of diseases and related health problems, 10th revision; MDAS, memorial delirium assessment scale; MMSE, mini–mental state examination.