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Hospitalisation costs and health related quality of life in delirious patients: a scoping review

Krankenhauskosten und gesundheitsbezogene Lebensqualität bei Patienten mit Delir: ein Scoping-Review

Chris van Lieshout[a,*], Ewoud Schuit[a], Carsten Hermes[b], Matthew Kerrigan[c], Geert W.J. Frederix[a]

[a] *Julius Center for Health Sciences and Primary Care, The Health Care Innovation Centre (THINC.) University Medical Center Utrecht, The Netherlands*
[b] *CCRN, Business economist (IHK), Co-founder of the German Delirium Network e.V., Bonn, Germany*
[c] *Independent HTA consultant, Ljubljana, Slovenia*

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ABSTRACT

Introduction: Delirium is a common condition of a global disturbance of cognition, triggered by underlying diseases. The objective of this study is to review the current evidence in the literature on direct healthcare costs and health-related quality of life (HRQOL) associated with delirium.
Methods: A systematic search was conducted in PubMed and Embase for relevant studies published between January 1, 2010 and November 4, 2021. Studies for inclusion reported estimates on healthcare costs or HRQOL, adjusted for relevant confounding factors.
Results: Fourteen studies on healthcare costs and eleven studies on HRQOL were included. Delirium resulted in (adjusted) increased costs ranging from $1,532 to $22,269 depending on included cost categories, the country and the type of hospital department. Increased length of stay for delirious patients ranged from 2.5 days to 10.4 days and had the largest contribution to overall, direct incremental costs. Heterogeneity was observed in HRQOL outcomes.
Conclusion: The analysis indicates that the presence of a delirium episode may lead to increased costs of hospitalisation. Changes in HRQOL due to delirium are not well demonstrated and more research is needed to determine the effect of delirium on HRQOL.

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ZUSAMMENFASSUNG

Einleitung: Das Delir ist ein häufiges Beschwerdebild, das durch eine globale Störung der Kognition charakterisiert ist und durch zugrunde liegende Erkrankungen ausgelöst wird. Ziel dieser Studie ist es, die aktuelle Evidenz zu den direkten Gesundheitskosten und zur gesundheitsbezogenen Lebensqualität („Health-Related Quality of Life", HRQoL) im Zusammenhang mit Delirzuständen zu sichten.
Methode: Die Datenbanken PubMed und Embase wurden systematisch nach einschlägigen, zwischen dem 1. January 2010 und dem 4. November 2021 publizierten Studien durchsucht. Eingeschlossen wurden Studien, die Schätzungen zu den Gesundheitskosten oder zur HRQoL (mit Adjustierung für relevante Störfaktoren) enthielten.

Abbreviations: AIDS, Acquired Immune Deficiency Syndrome; CAM, Confusion Assessment Method; CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; CAPD, Cornell Assessment of Pediatric Delirium; DOSS, Delirium Observation Screening Scale; DRS, Delirium Rating Scale; DSI, Delirium Symptom Interview; DSM-5, Diagnostic Statistical Manual of Mental Disorders, fifth edition; EQ-6D, EuroQol six-dimensional; HRQOL, Health Related Quality of Life; ICD, International Classification of Diseases; ICDSC, Intensive Care Delirium Screening Checklist; ICU, Intensive Care Unit; JBI, Joanna Briggs Institute; NeuroQOL, Quality of Life in Neurological Disorders; SAVR, Surgical Aortic Valve Replacement; SF-36, Short Form-36; TAVR, Transcatheter Aortic Valve Replacement; WHOQOLBREF, World Health Organization Quality of Life Abbreviated Version.

* Corresponding author. C. van Lieshout, MSc, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, PO Box 85500, 3508 GA Utrecht, The Netherlands.
E-mail: c.vanlieshout@umcutrecht.nl (C. van Lieshout).

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Ergebnisse: Eingeschlossen wurden 14 Studien zu Gesundheitskosten und 11 Studien zu HRQOL. In Abhängigkeit von berücksichtigten Kostenkategorien, Land und Krankenhausabteilung verursachten Delirzustände (adjustierte) Kostensteigerungen zwischen 1532 und 22 269 Dollar. Patienten mit Delir hatten um 2,5 bis 10,4 Tage verlängerte Krankhausverweildauern und den größten Anteil an den direkt zurechenbaren Gesamtkosten. Heterogenität ließ sich bezüglich der HRQoL-Outcomes beobachten.
Schlussfolgerung: Die Analyse zeigt, dass das Vorhandensein einer Delirepisode eine Steigerung der Krankenhauskosten verursachen kann. Veränderungen der gesundheitsbezogenen Lebensqualität infolge eines Delirs sind in den untersuchten Studien nicht hinreichend dargestellt; daher bedarf es weiterer Forschung, um die Auswirkungen eines Delirs auf die gesundheitsbezogene Lebensqualität zu bestimmen.

Introduction

Delirium is a decline in mental state, reduced clarity and a reduction of focus and attention according to the DSM-5 criteria [1]. Three subtypes of delirium can be distinguished: hyperactive delirium, hypoactive delirium, and mixed delirium. Hyperactive delirium is characterized as highly alert and uncooperative, whereas hypoactive delirium is more common and characterized by a lot of sleep, and inattentive disorganized thought. Mixed delirium is a form where there is a fluctuation between hyperactive delirium and hypoactive delirium. This is the most frequently observed type [2]. The onset of delirium can be triggered by infections, fever, alcohol withdrawal, major surgery, terminal phases of cancer or AIDS, and medications. Delirium can occur at any age, but is most commonly seen in the elderly and young children on ICU. Estimates of the incidence of delirium as a complication in adult ICU patients are between 19 and 82 percent [3,4]. Different standards, such as the International Classification of Diseases, tenth edition (ICD-10), the Diagnostic Statistical Manual of Mental Disorders, fifth edition (DSM-5), the Confusion Aassessment Method (CAM) and The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) were developed for Delirium detection [5–7].

Prevalence on hospital wards ranges from 7% to 27% depending on patient population and ward type (general surgical ward vs. geriatric ward and ICU), these figures might be an underestimation since delirium recognition is poor, only 12 to 35% of delirium patients are being recognised [3,8–10]. With use of validated assessment tools, recognition of delirium can be improved. This could result in a better management of delirium, which primarily consists of early recognition, and management of the underlying condition [11].

The burden of delirium is manifold, for patients, loved-ones and staff. For patients it may have an effect on mortality, morbidity, healthcare costs and health related quality of life (HRQOL) of patients. Gaining insight into the differences in costs and HRQOL is essential to further understand the impact of delirium and the potential for improvement of care. The aim of this review is therefore to summarize the available evidence on the impact of delirium on healthcare costs and HRQOL in hospitalized patients.

Methods

We performed a scoping review to summarize the available evidence on costs and impact on HRQOL of delirium. We adhered to the PRISMA statement for scoping reviews.

Inclusion criteria

Articles were eligible for this review if: 1) patients with delirium and without delirium were compared 2) the article provided information on HRQOL and/or hospitalisation costs. Studies were excluded when: 1) confounders were not investigated and/or adjustment for confounding was not conducted, 2) disease severity at baseline was not investigated, 3) hospital charges were not included, 4) studies were published in a language other than English 5) results were only presented in conference abstracts, and 6) studies on patients < 18 years.

Search

The MEDLINE and Embase databases were searched to find relevant primary articles from January 1, 2010 up to June 19, 2019. This search was updated on November 4, 2021 to extend the time window to November 4, 2021, in order to include the latest papers. Older papers were not included since costs are subject to change over time and the most relevant papers were of interest. For every database, a search strategy was defined with the support of an information specialist of the Utrecht University Library. Terms related to delirium, health care costs and HRQOL were searched in titles and abstracts of literature as well as in MeSH and Emtree terms. The complete search strategy is provided in the Appendix A.

Study selection

After removal of duplicates, the title and abstract of the obtained studies were screened for the eligibility criteria by a single researcher. The full texts of articles were assessed when needed, for clarification. If results were published multiple times, data from the most complete article was used.

Data collection

Data were extracted from each included article on: study design and period, study setting and country, number of included participants with percentage experiencing delirium, populations characteristics; including age and gender, delirium assessment tool, covariates and time of measurement. Data extraction was conducted by one researcher, and reviewed by another.

For cost studies, the cost category and the differences in costs in the presence of delirium were reported as well as the general extracted information listed. Studies that reported on costs specified by type of costs were summarized in a separate table. No critical appraisal of the calculations that derived the costs included in the studies was performed. If the year of the cost analysis was reported in the original papers, cost estimates were converted to 2020 US Dollars with use of consumer price indeces and currency exchange rates. The studies that were identified that reported healthcare costs were also screened for data on length of stay for delirious and non-delirious patients.

For the studies on HRQOL, the measurement tool and differences in outcome were extracted in addition to the study characteristics listed above. Studies which reported on the differences for each of the eight domains of the SF-36 were summarized.

Risk of bias

Possible confounders and adjustment for confounding were evaluated during the study selection part of this study; studies were excluded if no attempt was made to adjust for confounding.

Results

Study selection

The first systematic search identified 931 studies, after the removal of duplicates. After screening titles and abstracts, 58 studies remained for full text screening, of these, 18 studies were included. The updated resulted in a further 839 papers, included duplicates with the first search, of which seven were included. Across the initial and updated search, fourteen of the included studies reported costs [12–25] and eleven reported data on HRQOL [26–36] (Figure 1). The most frequent reasons for exclusion during the full text screening were related to papers not concerning costs or HRQoL of Delirium (wrong outcome) and no or inappropriate adjustment for confounding. In the included papers on costs the prevalence of delirium ranged from 1.61% to 78.5% in these studies, combining figures from regular wards and ICUs. The majority of analysis were from the United States of America (9/14 in Costs, 5/11 in HRQOL). The assessment tools for delirium that were used in cost studies identified were: Confusion Assessment Method (CAM) (4, 29%), Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (4, 29%), ICD-9 codes (4, 29%) and the Delirium observation screening scale (DOSS) (2, 14%). For the HRQOL papers the used assessment tools were: CAM-ICU (6, 55%), Intensive Care Delirium Screening Checklist (ICDSC) (2, 18%), Delirium symptom Interview (DSI) (1, 9%), Delirium Rating Scale (DRS) (1, 9%), and Delirium observation screening scale (DOSS) (1, 9%). All of these assessment tools have been validated [37,38].

Healthcare costs

In Table 1, study characteristics are given for the 14 included studies that reported costs. In the study of Potter *et al.* (2018), costs were stratified by intervention; resulting in two costs estimates from this study [13]. Four studies, Potter *et al*, Ha *et al* and the two Kwak *et al* papers identified cases only by previously registered ICD-9 code. Nine studies retrieved data from existing databases, the remaining 5 articles looked at data prospectively. The majority of included papers (11 out of 14) based costs on direct healthcare costs and not on reimbursement, the other three did not specify the origin of the figures used.

Studies were conducted in different countries, and costs were reported in in each national currency; all currencies were converted to US Dollars. Table 2 shows these amounts in the original currency with and in 2020 US Dollars. Exchange rates were accurate to two decimal places. An inflation rate was not taken into account. Costs were higher amongst patients with delirium in all studies. Unadjusted incremental healthcare costs (range $3,191 to $27,491) were higher than adjusted incremental costs: adjusted estimates ranged from $1,532 to $22,269.

Three studies stratified data by the type of costs. Ha *et al.* (2018) reported healthcare costs by category only in a figure, therefore values could not be derived from that study [14]. For the other studies, costs are given by cost category in Table 3. In the remaining two studies, the highest proportion of costs was made up of routine care, generally *per diem* hospital charges. The study of Vasilevskis, et al. (2018) gave estimates corrected for confounding; all costs were higher for patients with delirium compared with those without delirium [15].

All but two papers also reported the hospital length of stay for delirious and non-delirious patients (12-14, 16-23, 25). Potter *et al.* (2018) reported costs split by the procedure that led to hospitalization (SAVR and TAVR) and Schubert *et al.* (2018) reported detailed information on hospital length of stay for different subgroups (Table 1) [13,18].

Health related quality of life

Eleven articles that assessed HRQOL were included in this review. Study characteristics are presented in Table 4, with delirium prevalence ranging from 8% to 56% on regular wards and ICUs. All of the studies collected data within prospective cohort studies.

In this review HRQOL was measured with different tools: the EuroQol five-dimension instrument (EQ-5D) (used once), Short Form-36 (SF-36) (used four times), SF-12 (used once), Neuro-QOL (used twice), and WHOQOL-BREF (used once). Seven of the 11 studies found statistically significant differences in HRQOL between patients with delirium and without delirium ($p < 0.05$). All differences were towards a lower HRQOL when delirium was detected.

Four of the included studies used the SF-36 for HRQOL assessment. These 4 studies evaluated the 8 domains of the SF-36 separately. In Table 5, differences in QOL by domain of the SF-36 are shown for patients with delirium episode versus patients without delirium. When differences were statistically significant, they indicated that delirium led to a decrease in HRQOL in all cases. However, there were some discrepancies in HRQOL when examining all estimates, regardless of statistical significance. Except for the domain on vitality, all significant estimates indicate a decrease in HRQOL when delirium was detected.

Discussion

In this review we found a potential meaningful difference in hospitalisation costs between patient having a delirium episode and those who had not. In contrast to the studies on healthcare costs, HRQOL changes due to delirium were not consistent between studies, although results may suggest a decrease in HRQOL in patients with delirium.

The diagnosis of delirium is frequently missed, only 12 to 35% of delirium cases are recognized during hospital stay [3,39,40]. In particular for studies that reviewed patient record databases; screening of delirium might not have been performed (or noted) and screening might only be considered when delirium was suspected. Not all cases of delirium would therefore be recognized and be present in the patient record databases. This might result in overestimation of the costs estimates based on patient record databases.

Hospitalisation costs were stratified by cost type in two studies, in order to determine the component that contributed most to the increase in total hospitalisation costs [15,20]. Clinical admissions resulted in the highest costs of the evaluated cost components. One study (Vasilevskis, *et al.* 2018) provided adjusted estimates [15]. Not all studies included the same costs for their estimates. Some studies only included costs that contributed to an increased length of stay, whereas other studies looked at hospital charges between patients with delirium and without delirium. Hospital reimbursement charges might give a better reflection of other additional underlying costs such as diagnostics and therapeutics. Increased length of stay is only a part of overall total hospitalisation costs.

The question whether the additional costs of delirium are reimbursed is very much related to the health system and country in question [41]. There are some indications that the additional workload for patients with delirium is not recognized by default with common scores and therefore the costs are not reimbursed [40,42].

Table 1
Study characteristics and incremental costs in the presence of delirium. If reported, age and gender are shown by D = delirium; ND = no delirium.

Reference (year)	Country	Study design	Inclusion period participants	Delirium assessment tool	Setting	N (% delirious)	Age in years (mean ± SD or median [IQR])	Men (%)	Covariates/ stratified by	Costs included	Crude incremental costs*	Adjusted incremental costs *	Length of Stay (days)
W.A. van Eijsden, et al. (2015) [12]	Netherlands	Retrospective study on prospective collected data	Feb.2013 - Dec. 2014	DOSS	Surgery for critical limb ischemia	92 (32%)	ND 75 [69–80]; D 81 [76–86]	ND 57%; D 59%	Visual impairment and diabetes mellitus	Hospital stay costs	$3,191 (95% CI: $865 -$5,518)	$2,209 (95% CI $1,043 - $4,522)	ND: 8 D: 14 Δ: 6
B.J. Potter, et al. (2018) [13]	US	Retrospective analysis of administrative data	Fiscal year 2015	ICD-9-CM code 293.0	TAVR	12114 (1.61%)	87.06 ± 3.77	51%	Demographics, comorbidities, complications, and Charlson's index	Hospitalization costs	$27,095 (95% CI: $18,275-$35,914)	$15,140 (95% CI: $10,280 - $19,979)	ND: 6.1 D: 11.9 Δ: 5.9
					SAVR	8974 (3.60%)	84.2 ± 2.67	61%			$27,491 (95% CI: $21,924 –$33,553)	$18,191 (95% CI: $14,391-$21,992)	ND: 10.4 D: 17.0 Δ: 6.6
A. Ha, et al. (2018) [14]	US	Retrospective cohort study Premier hospital database	2003-2013	ICD-9 codes	Urologic cancer surgery	Weighted population 1097335 (2.7%)	Most frequent in group 60-69	87%	Patient, hospital, and perioperative characteristics.	Direct hospital costs	Median $8,822	$2,997(IQR: $2,500 – $3,493)	ND: 3 D: 7 Δ: 4
E. E. Vasilevskis, et al. (2018) [15]	US	Prospective cohort	NA	CAM-ICU	BRAIN-ICU	479 (78.5%)	57 ± 15	52%	Insurance status, age, Charlson comorbidity score, pre-existing cognitive dysfunction, and APACHE II at enrolment, daily modified SOFA, daily severe sepsis status, daily mechanical ventilation status, day of ICU stay.	30 days ICU stay, mean incremental cumulative ICU costs in survivors	NA	Total costs: $22,269 (95% CI $13,897-$29,333) attributed to intensity of utilization; attributed to mortality $5,707 ($2,567–$9,824)	Not Reported

Table 1 (*Continued*)

Reference (year)	Country	Study design	Inclusion period participants	Delirium assessment tool	Setting	N (% delirious)	Age in years (mean ± SD or median [IQR])	Men (%)	Covariates/ stratified by	Costs included	Crude incremental costs*	Adjusted incremental costs *	Length of Stay (days)
J.Y. KIM, et al. (2017) [16]	Korea	Retrospective analysis of data	2010-2014	Short version of CAM	Osteoporotic hip fracture	74 (50%)	ND 80.8 ± 6.7; D 81.8 ± 6.8	ND 42%; D 48%	Matching	Infrastructure, medications, materials, instruments, fees of the surgeon, anesthesiologist, consulting physician, and so on. Converted from Won to US dollars, applying mean exchange rate in June 2015.	NA	$1,532 (p-value = 0.017)	ND: 16.7 D: 20.2 Δ: 3.5
M.G. Zywiel, et al. (2015) [17]	Canada	database review	Jan. 2011 - Dec. 2012	CAM	Surgery acute hip fracture	242 (48%)	ND 79.8 (range 65-101); D 85.3 (range 65-103)	ND 32%; D 29%	Propensity matching	Infrastructure, material, and labor costs	$9,661 (p-value < 0.001)	$9,342 (95% CI $4,160 -$14,522)	Total: ND: 11.2 D: 18.5 Δ: 7.3 Post-Op: ND: 9.7 D: 16.6 Δ: 6.9
M. Schubert, et al. (2018) [18]	Switzerland	database review	Jan. 2014 - Dec. 2014	DOSS and/or ICDSC	Hospital	10906 (28.1%)	ND 67.3 ± 15.2; D 68.4 ± 15.8	ND 58.7%; D 61.1%	Age, gender, pre-admission residence type, admission type, Charlson co-morbidity index, type of service, and ICU stay	Total costs per case (no further information)	$21,026 (95% CI $20,020 – $22,032)	$10,060 (95% CI $9,356 – $10,664)	Stratified by disease ranging from ND: 5-8 D: 17-71
K.J. Moon, et al. (2013) [19]	Korea	Prospective cohort study (?) Baseline info of electronic medical records	Sept. 2009 - Apr. 2012	CAM-ICU	MICU/SICU	3101 (20.5%)	ND 58 ± 15.7; D 68 ± 14.9	ND 58.4%; D 56.3%	Age, gender, BMI, APACHE II score, surgery, admission via the ED, use of ventilator, and infection	medical costs related to the hospitalization event	** $7,869 (p < 0.001)	** $5,031 (SE $826)	Total: ND: 22.5 D: 32.9 Δ: 10.4 ICU: ND: 3.2 D: 7.7 Δ:4.5

Table 1 (*Continued*)

Reference (year)	Country	Study design	Inclusion period participants	Delirium assessment tool	Setting	N (% delirious)	Age in years (mean ± SD or median [IQR])	Men (%)	Covariates/ stratified by	Costs included	Crude incremental costs*	Adjusted incremental costs *	Length of Stay (days)
C.H. Brown, et al. (2016) [20]	US	prospective observational study nested in randomized trial	Oct. 2012 - Feb. 2014	CAM or chart review	cardiac surgery	66 (56%)	ND 69 ± 8; D 70 ± 7	ND 79.3 D 75.7%	Propensity score model	Charge data	Median $11,716(p = 0.02)	Median $11,489 (95%CI $2,187-$20,789, P = 0.02)	ND: 6 D: 9 Δ: 3
C.H. Brown, et al. (2016) [21]	US	Prospective cohort study	Feb. 2012 - July 2014	CAM-ICU or chart review	Spine surgery	89 (40.5%)	ND 74 [IQR 71-77]; D 75 [IQR 72-78]	ND 56.6%; D 46.2%	Age, functional status, ASA risk score, surgery length, intra-operative red blood cell transfusion, return to the operating room, and complication	Charge data	Median $20,408	OR 3.49 (95 CI 1.33-13.2) for being in higher quintile	ND: 7 D: 9.0 Δ: 2.5
M.K. Kwak, et al. (2020) [22]	US	Retrospective observational study	2011-2014	ICD-9-CM	TAVR	7087 (8%)	65-79 (28.96%) 80 -89 (55.31%) > = 90 (15.72%)	3664 (51.77%)	Demographics, comorbidi-ties,LoS	Total Hospital Costs	NA	Delirium only $82,598 (95% CI 78,149-87,047)	ND 7.5 D13.1 Δ:3.04
M.K. Kwak, et al. (2021) [23]	US	Retrospective observational study	2011-2014	ICD-9-CM	Acute Heart Failure Exacerbation	2,826,131 (4.53%)	65-79 (45.73%) 80 -89 (39.89%) > = 90 (14.38%)	1.296,65 (45.88%) D = 59,256 (4.45%)	in-hospital mortal-ity/length of stay	Total Hospital Costs	NA	$4,315 (95% CI, $4,052-4,577)	ND:5 ± 4.03 D:8.04 ± 6.92 Δ:3.04
R.Y. Gou, et al. (2021) [24]	US	Prospective cohort study	2010-2014	CAM	SAGES	497 (25%)	76.8 ± 5.1	216 (43%)	Age, gender, admission type, Charlson co-morbidity, ASA, IQCODE, Type of sergery	Adjusted cumulative health care costs per patient	NA	$20,581	NA
S. Cai, et al. (2020) [25]	US	Retrospective database review	Jan. 2017 – Dec. 2018	CAM-ICU	Cardiac Surgery	301 (24.25%)	ND 50.46 ± 12.32; D 51.27 ± 12.08	ND = 179 (78.51) D = 56 (76.71)	Age, gender, pre-admission residence type, admission type, Charlson co-morbidity, sedatives	Total Hospital Costs	NA	$11,160 ± $2,550 (95% CI, $6,140-$16,490, p< 0.001)	ICU LOS, days D = 11.52 ± 10.14 ND = 7.22 ± 8.17 Δ: 4.30 ± 1.19

APACHE = Acute Physiology and Chronic Health Evaluation; BMI = body mass index; CAM = Confusion Assessment Method; CAM-ICU = Confusion Assessment Method for the Intensive Care Unit; CI = confidence interval; DOSS = Delirium Observation Screening Scale; ED = Emergency Department; ICDSC = Intensive Care Delirium Screening Checklist; ICU = intensive care unit; IQR = Interquartile Range; LOS = length of stay; MD = Median;MICU = Mobile Intensive Care Unit; PICU = Pediatric Intensive Care Unit; PRISM = Pediatric Risk of Mortality; SAGES = Successful Aging after Elective Surgery; SAVR = surgical aortic valve replacement; SOFA = Sequential Organ Failure Assessment; TAVR = Transcatheter aortic valve replacement.

* Costs recalculated to 2020 US Dollar using Consumer Price Index (source: https://fred.stlouisfed.org/series/CPIAUCNS).

** No year of costs reported, conversion to 2020 US Dollar not possible.

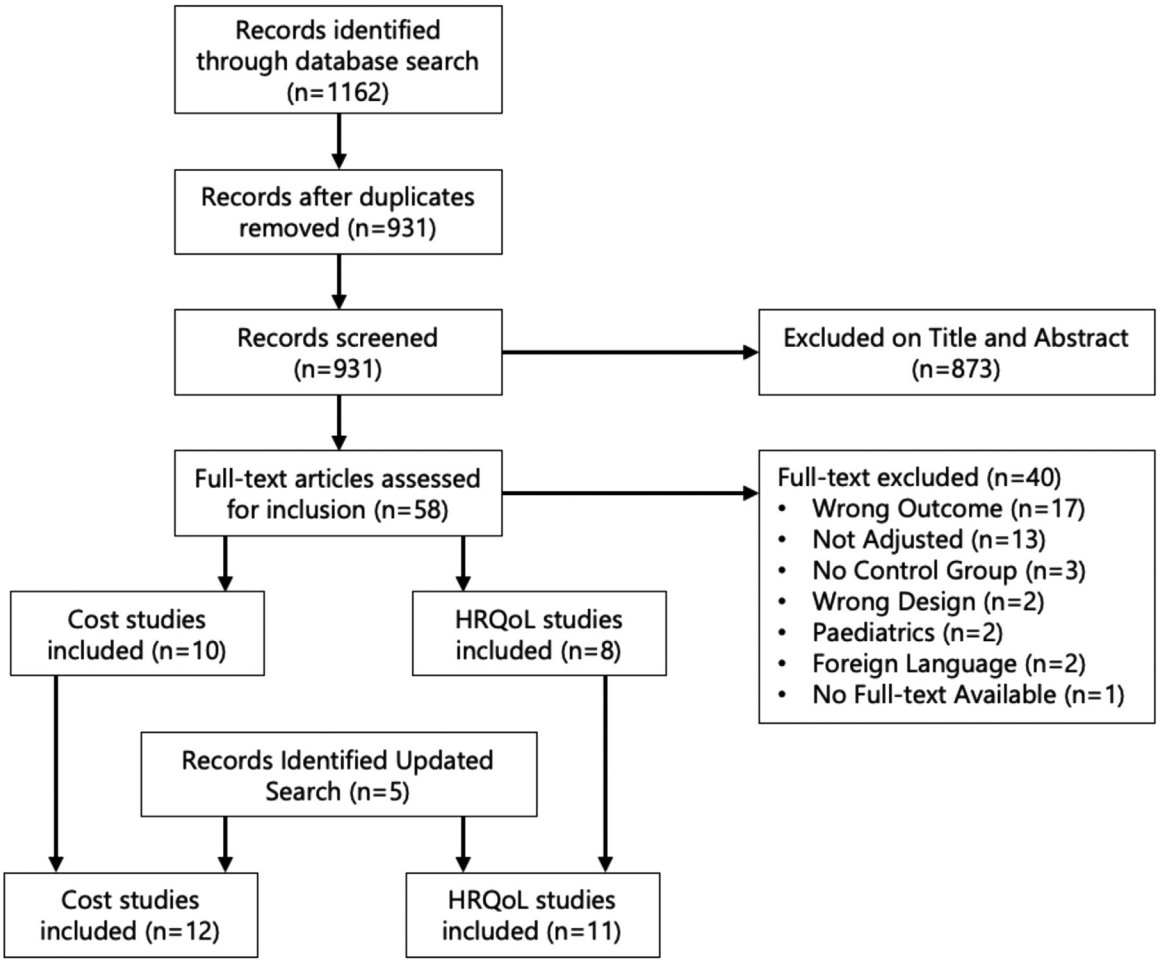

Figure 1. Flow diagram of study selection.

Table 2
Converted amounts to US dollars. Exchange rates were accurate to two decimal places.

	Year conversion	Exchange rate	Original amount of crude estimate	Converted amount crude estimate	Original amount of adjusted estimate	Converted amount adjusted estimate
W.A. van Eijsden, et al. (2015) [12]	2014	1.33	€2,195 (95% CI: €595 – €3,794)	$2919 (95%-CI: $791 - $5,046)	€1,519 (95%-CI: €7,17 - €3,110)	$2,020 (95%-CI: $954 – $4,136)
M.G. Zywiel, et al. (2015) [17]	2012	1.00	8,569 CAD	$8569	8286 CAD (95%-CI: 3690 - 12881)	$8286 (95%-CI: $3,690 - $12,881)
M. Schubert, et al. (2018) [18]	2014	0.92	20,900 CHF (95% CI 19,900 – 21,900)	$19228 (95%-CI: $18,308 – $20,148)	10,000 CHF (95%-CI: 9,300 - 10,600)	$9,200 (95%-CI: $8,556 – $9,752)

CAD = Canadian dollar; CHF = Confoederatio Helvetica Franc; CI = confidence interval.

Table 3
Incremental costs for ever delirious vs never delirious by cost type. All converted to 2020 US Dollar.

Reference	E.E. Vasilevskis, et al. (2018) [15]	C.H. Brown et al. (2016) [20]
Total costs	$22,269 (95%-CI: $13,897 - $29,333)	$11,366
Pharmacy	$5,016 (95%-CI: $3,223 - $6,266)	$556
Laboratory	$1,479 (95%-CI: $673 - $2,555)	$2,910
Radiology	$830 (95%-CI: $466 - $1,283)	$743
Therapy	$1,129 (95%-CI: $649 - $1,672)	$1,346
Supplies	$3,039 (95%-CI: $1,987 - $4,031)	- $423
Routine	$17,433 (95%-CI: $10,859 - $24,289)	$4,362
Miscellaneous (diverse)		$1,395
operating room	NA	$1,966
Costs per day		
Unit	Incremental costs attributed to intensity of utilization	Difference median costs (unadjusted)

Table 4
Study characteristics and quality of life (QOL) for delirium. If reported, age and gender are shown by D = delirium; ND = no delirium.

Reference	Country	Study design	Inclusion period participants	Setting	Age in years (mean ± (SD) or median [IQR])	Men (%)	N (% delirious)	Delirium assessment tool	Covariates	QoL (time)	Difference in QOL
J.M. Humphreys, et al. (2017) [26]	Australia	Prospective cohort study	Apr. 2003 – May 2011	CABG surgery	63.5 ± 10.1	82.2%	173 (35%)	DSI	Age, gender, indigenous and Australian peoples, alcohol use, comorbidities, urgent surgery, left ventricular ejection fraction, time spend on the aortic cross-clamp, and baseline QOL	SF-36 (Prior surgery, day 4, six months. (Not clear which measurement is used))	General health (beta -0.22)
A.E. Wolters, et al. (2014) [27]	The Netherlands	Prospective cohort study	July 2009 – Aug. 2011	ICU	ND 59.4 ± 16.6; D 60.5 ± 16.7	ND 58.9%; D 65.8%	1101 (37%)	CAM-ICU	Gender, APACHE IV, type of admission, and CumSOFA	EQ-6D (12 months)	-0.04 (p-value = 0.09)
A.M. Naidech, et al. (2013) [28]	US	Prospective cohort study	Dec. 2009 – Apr. 2013	Neuro/spine ICU	ND 61.7 ± 14.6; D 63.9 ± 12.1	54%	114 (27%)	CAM-ICU	Age, NIHSS on admit, any BZD use.	Neuro-QoL (day 28, 3 months, and 12 months)	Applied cognition and executive function (estimate 5.8, 95% CI 0.15 to 11.5) and fatigue (estimate 7.4, 95% CI 1.7 to 13).
L.J. Rosenthal, et al. (2017) [29]	US	Prospective cohort study	Dec. 2009 – Oct. 2014	Acute ICH	61	59%	81 (36%)	CAM-ICU	Age, NIHSS, time of assessment	Neuro-QOL (day 28, 3 months, and 12 months)	Mean difference with agitation at day 28: 15.7; at 12 months: 23.5. Difference without agitation at day 28: 10; at 12 months: 2.5
F.J. Abelha, et al. (2013) [30]	Portugal	Prospective cohort study	Nov. 2008 – Aug. 2009	SICU	66 [54–74]	63%	358 (16% of 562 with delirium assessment)	ICDSC	Age, gender, ASA physical status, BMI, duration of anesthesia, type of anesthesia, locoregional anesthesia, emergency surgery, temperature at SICU admission, troponin I at SICU admission, comorbidities, high-risk surgery, total RCRI, crystalloids, colloids, erythrocytes, fresh frozen plasma, platelets, and APACHE II scores	SF-36 (before and at 6 months)	Physical functioning (beta 17.402), vitality (beta 8.221) and social function (beta 16.802)

Table 4 (*Continued*)

Reference	Country	Study design	Inclusion period participants	Setting	Age in years (mean ± (SD) or median [IQR])	Men (%)	N (% delirious)	Delirium assessment tool	Covariates	QoL (time)	Difference in QOL
J.R. Basinki, et al. (2010) [31]	US	Prospective cohort study	1997-1999[36]	Hematopoietic cell transplant	ND 22-35 most frequent; D 36-45 most frequent	ND 65.5%; D 43.5%	52 (44%)	DRS	6 months: physical component: cell type; 12 months mental component: age	SF-12 (6 months, and 12 months)	6 months: physical component (-7.26); 12 months mental component (-4.75)
M. van den Boogaard, et al. (2012) (32)	Netherlands	Prospective cohort study	Feb. 2008 – Feb. 2009	ICU	ND 65 [57–72]; D 65 [58–75]	ND 68%; D 60%	915 (19%)	CAM-ICU	gender, urgent admission, APACHE II score, sepsis, and length of intensive care unit stay	SF-36 (at median 18 months)	All domains not significant
C.M. Abraham, et al. (2014) [33]	US	Prospective cohort study	NA	trauma ICU	42.4 ± 16.7	55.7%	115 (17%)	CAM-ICU	Age, sex, comorbidities, and ISS	SF-36 (12 months)	All domains not significant
L.K. Larsen, et al. (2020) [34]	Denmark	Observational cohort study	Aug. 2015 – June 2016	Acute Brain Injury	61 [51–69]	53%	47 (83%)	ICDSC	RBANS, VAS, GCS, COMA, SAPS, APACHE, Charlson Comorbidity Index	EQ-5D	All domains not significant
T.L. Janssen, et al. (2021) [35]	Netherlands	Prospective cohort study	Nov. 2015 – June 2018	Colorectal Cancer Surgery or Abdominal Aortic Aneurysm Surgery	76 [73–81], D = 78 [74–85], ND = 76 [73–81]	171 D = 14 ND = 157	264 (7.9%)	DOS + DSM-IV	MMSE, CES-D, Male, gender, Age, Sugery, KATZ-Adl, SNAQ History of Patient incl. Delirium	WHOQOL-BREF(discharge, 6 months, 12 months)	At 12 months significant decrease across all domains.
C.L. DeBolt, et al. (2021) [36]	US	Prospective cohort study	2010 – 2016	NA	57 ± 12 D = 57 ± 11 ND = 57 ± 12	D = 12.76%	236 (14.4%)	CAM-ICU	Age, gender, Race, BMI, FEV, LoS, Bypass time, 6MWD)	SF-12 (3,6,12,18, 24,30 and 36 months)	SF12-PCS -4.0; (95%CI: – 7.4 to – 0.7) SF12-MCS 2.2; (95%CI: – 0.7 to 5.7)

APACHE = Acute Physiology and Chronic Health Evaluation; ASA = American Society of Anesthesiologists; BMI = body mass index; CABG = Coronary Artery Bypass Grafting; CAM = Confusion Assessment Method; Cum-SOFA = cumulative total daily Sequential Organ Failure Assessment; DRS = Delirium Rating Scale; DSI = Delirium Symptom Interview; ICU = intensive care unit; IQR = Interquartile Range; ISS = Injury Severity Score; n = number of subjects; NIHSS = National Institutes of Health Stroke Scale; RCRI = Revised Cardiac Risk Index; SD = Standard Deviation; SF-12 = 12-Item Short Form Health Survey; SF-36 = 36-Item Short Form Health Survey; SICU = surgical intensive care unit.

Table 5
Differences in SF-36 domains between patients with delirium and patients without delirium.

SF-36	Humphreys, et al. [26]	Abelha, et al. [30]	Boogaard, et al. [32]	Abraham, et al. [33]
	Beta	Beta	Median	Beta
Physical functioning	0,09	17,402*	-20	-0,17
Social functioning	0,13	16,805*	-13	-0,08
Physical health	0,04	NA	-25	-0,08
Emotional problems	-0,14	NA	0	0,04
Mental health	0,06	NA	-8	0,03
Vitality	-0,12	8,221*	-5	-0,003
Bodily pain	-0,1	NA	0	0,01
General health perception	-0,22*	NA	-5	0,001
Direction	Negative, worse	Predictor poor results	Negative, worse	Negative, worse

* Indicates significant differences p-value < 0.05.

Even though the costs reported in each of the studies is different, evidence for increased health care costs for patients with delirium is consistent among studies, indicating that health care costs are very likely to be increased when delirium was detected. Hospital length of stay was longer for patients with delirium, with the exception of one cardio thoracic surgery study by Brown *et al* [20]. The question remains what the drivers of added costs are. The additional admission days could have several different reasons such as additional time required for the treatment of the delirious episode, additional time required for treatment of the underlying illness due to delirium or the occurrence of complications due to delirium.

Different measurement tools were used to obtain HRQOL estimates, with the SF-36 as the most frequently used tool in this review. Estimates for each of the eight dimensions of the SF-36 could be retrieved from the included studies that used the instrument. Statistically significant differences were found in the domains of physical functioning, social functioning, vitality and general health perception; indicating worse HRQOL for patients with delirium. For vitality, all estimates were worse for patients with delirium without being statistically significantly different in each study. However, for all other domains (physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health), the results showed a mixed pattern, pointing towards both a negative and a positive association [26,30,32,33]. Given the reduction in consciousness, focus and attention, a decrease in HRQOL could be expected.

Strengths and limitations

A strength of this analysis is that it provides a single overview of the impact delirium can have on healthcare costs and HRQOL. A single overview of costs and HRQOL outcomes can help in better understanding of the effects delirium on patients. The combination of these outcomes may also prove to be useful for future health economic evaluations.

A limitation could be the absence of evidence synthesis. The synthesis was not performed due to multiple challenges: 1) cost charges might differ for the same procedures between countries and settings, 2) different settings were included in this review; 3) delirium might have a different impact in each setting. A different limitation could be the limited number of search terms and the limited time window used for delirium papers, which may have reduced the number of records found.

In this analysis no formal evaluation of the risk of bias was performed. Some of the included studies did not adjust for characteristics such as disease severity. These studies may have a high risk of bias and might have been removed if a formal evaluation of risk of bias was performed. However, by excluding these studies, the analysis of the remaining studies would result in insufficient data to report possible outcomes. In future research the adequate analysis and mitigation of confounders should be carefully considered as this may lead to a better insight on how total costs differ in different countries, settings and patient groups.

Conclusions

Patients experiencing delirium during hospital may incur increased hospitalisation costs mainly due to increases in length of stay. An overview of HRQOL outcomes in delirious patients showed ambiguity in outcomes with a suggestion towards a decrease in HRQOL in delirious patients. Well designed, prospective studies into healthcare costs and HRQOL in delirious and non-delirous patients may allow for stronger conclusions.

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CRediT author statement

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.zefq.2022.02.001.

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