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## Hospital costs of post-operative delirium: A systematic review

Md. Parvez Mosharaf

*University of Rajshahi*, parvezstatru@gmail.com

Khorshed Alam

*University of Southern Queensland*, khorshed.alam@usq.edu.au

Nicholas Ralph

*University of Southern Queensland*, Nicholas.Ralph@usq.edu.au

Jeff Gow

*University of Southern Queensland and University of KwaZulu-Natal*, gowj@usq.edu.au

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## Hospital costs of post-operative delirium: A systematic review

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**Authors**

Md. Parvez Mosharaf  
University of Rajshahi

Khorshed Alam  
University of Southern Queensland

Nicholas Ralph  
University of Southern Queensland

Jeff Gow  
University of Southern Queensland and  
University of KwaZulu-Natal

**Corresponding author**

Md. Parvez Mosharaf  
University of Rajshahi  
parvezstatru@gmail.com

# Hospital costs of post-operative delirium: A systematic review

**Abstract**

**Aims:** In this systematic review, the primary aim is to investigate the hospital cost burden attributed to post-operative delirium (POD). A secondary aim is to examine how patient length of stay (LOS) in hospital varies across the selected studies.

**Background:** POD is a common occurrence after major surgery and leads to serious medical complications. It is associated with increased morbidity and double the risk of mortality from surgery compared to non-delirious patients. POD increases patient LOS in hospital and increases the economic burden on patients and the health system.

**Design:** A systematic review was conducted.

**Method:** Published articles in English over the period 2010 to 2020 were searched using the PubMed and MEDLINE databases. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. The study quality and risks of bias of included studies were assessed using the Newcastle–Ottawa Quality Assessment Scale (NOS).

**Results:** A total of 2539 published records were initially screened and ultimately ten studies were found to be relevant to the review criteria. Six studies were from the United States of America (USA) and the others from South Korea, Australia, and Canada. The additional costs for patients with POD ranged from a minimum of US\$1551 to a maximum of US\$23 698 compared to non-delirious patients. Costs were higher in the USA than other countries. Studies reported most surgical patients experiencing POD were aged 70 years or older which dramatically increases the risk of its occurrence and increases LOS and hospital related costs. The difference in LOS between POD and non-delirious patients ranged from 0.8 to 7.3 days and this increased significantly if POD patients were in intensive care.

**Conclusions:** Increased LOS and increased hospital costs are strongly associated with POD after major surgery.

**Keywords:** post-operative delirium, POD, length of stay, LOS, costs, systematic review

**Introduction**

Among post-operative medical complications, delirium is common and characterised by cognitive dysfunction, inattention and thinking disorder.<sup>1,2</sup> Delirium has two states – hyperactive and hypoactive.<sup>3</sup> Post-operative delirium (POD) is significantly associated with higher risk of morbidity and mortality, inferior functional recovery and extended immobilisation.<sup>3,4</sup> The major factors in developing POD

are advanced age, previous history of mental dysfunction, multiple medical comorbidities, acute injuries and pain.<sup>1,5–8</sup> Recent reviews of its incidence reveal a wide range from 3.3 to 77 per cent among surgical and intensive care unit (ICU) patients.<sup>9–12</sup> Studies report that POD also leads to prolonged length of stay (LOS) in hospital and ICU, and associated increased cost of health care treatment both in hospital and after discharge.<sup>13–19</sup>

The overall additional estimated cost for delirium was reported as ranging from US\$806 to US\$24 509 in 2019.<sup>20</sup> In 2021, a study in the USA reported the health care costs attributed to POD after major elective surgery for delirious patients in one year had a mean of US\$146 358 (SD: US\$140 469) which is significantly higher than US\$94 609 (SD: US\$80 648) for non-delirious patients. The annual national health care costs in the USA due to POD were estimated at US\$32.9 billion (CI 95%: US\$25.7 billion–US\$42.2 billion).<sup>21</sup> An Australian study described that the cost index of hospital episodes for post-operative delirious patients was 51 per cent higher than the non-delirious patients. Post-operative delirious patients also had a higher 28-day rehospitalisation rate than their counterparts.<sup>22</sup> Total cost due to delirium was about AU\$8.8 billion in 2016–2017 and this severe neuropsychiatric syndrome causes about 10.6 per cent of cognitive impairment (i.e. dementia) in Australia.<sup>23</sup>

POD also increases LOS in hospital and ICU and can lead to other post-operative complications. Increased LOS in hospital and ICU attributed to POD after major surgery is significantly higher than for non-delirious patients.<sup>24–27</sup> Further, hospital readmission after initial discharge was also higher among patients with cognitive impairments like POD.<sup>28</sup> As the prevalence of POD in ICU is upwards of 80 per cent, an investigation of the cost of POD and the resultant extended LOS is needed.<sup>29</sup>

Research evidence shows that POD is a potentially preventable medical condition.<sup>30–32</sup> The occurrence of delirium could be avoided for 30 to 40 per cent of medical emergency patients.<sup>33</sup> Considering the severe impact on patient's morbidity and mortality, the prevention of POD is essential to minimise the risks to

the individual surgical patient and to mitigate the economic burden on the patient, health system and society.<sup>34,35</sup>

## Aims

The primary aim of this study was to systematically review the literature on the hospital costs of POD over the period 2010 to 2020. A secondary aim was to examine how patient LOS in hospital varies across the selected studies.

## Methods

### Review design

This review involved a systematic search of studies in the PubMed, PubMed Central and Medline databases and followed the standard Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>36</sup> All published research articles related to delirium and post-operative delirium (POD) including reviews and meta-analysis were taken into consideration based on MeSH terms and keywords related to cost and hospital stay.

### Search strategy

Of the published journal articles from 2010 to end of 2020, articles were only included if they were peer-reviewed research articles, available as full-text, written in English and reported on one or more of the following: the post-operative delirium condition, any associated direct or indirect hospital costs, the length of stay in hospital or ICU.

The systematic literature searching occurred in two electronic databases of PubMed, and PubMed Central, and Medline. MeSH terms, key words and subject headings were used which are conceptually synonyms of delirium, POD and the direct or indirect hospitalisation cost. The OR/AND operator was used to create the

combination of searching key words. The following MeSH terms and key words with a combination of delirium and POD were used to search the literature: “economics”; “health care economics and organizations”; “cost of illness”; “cost evaluation”; “cost-benefit analysis”; “health care costs”; “cost Analysis”; “cost effectiveness”; “statistics and numerical data”; “economic outcome”; “economic impact”; “medical expenditure”; “cost utility”; “costs and cost analysis”; “hospital costs”; “medical care cost”; “delirium/statistics and numerical data”; “emergence delirium/statistics and numerical data”; “care, post-operative”; “length of stay”. All the outcomes were recorded and assessed through the various filtration steps according to PRISMA guidelines and the final articles were selected.

### Eligibility/inclusion criteria

The preliminary outcomes of interest were increased LOS in hospital and ICU due to POD and the additional costs of hospitalisation related to POD.

Studies that did not satisfy the inclusion criteria were excluded. Moreover, published articles not in English, systematic reviews, meta-analyses, editorials, conference proceedings, commentaries and research protocols related to delirium were also excluded.

### Screening process

For this systematic review, the direct and indirect cost data and the LOS information of delirious patients were collected from selected full-length research articles written in English. To perform this, the outcome records from the database search were evaluated by two independent researchers screening the title, abstract and the full-length articles to select the most relevant studies. This was done using the PRISMA guidelines. The first researcher

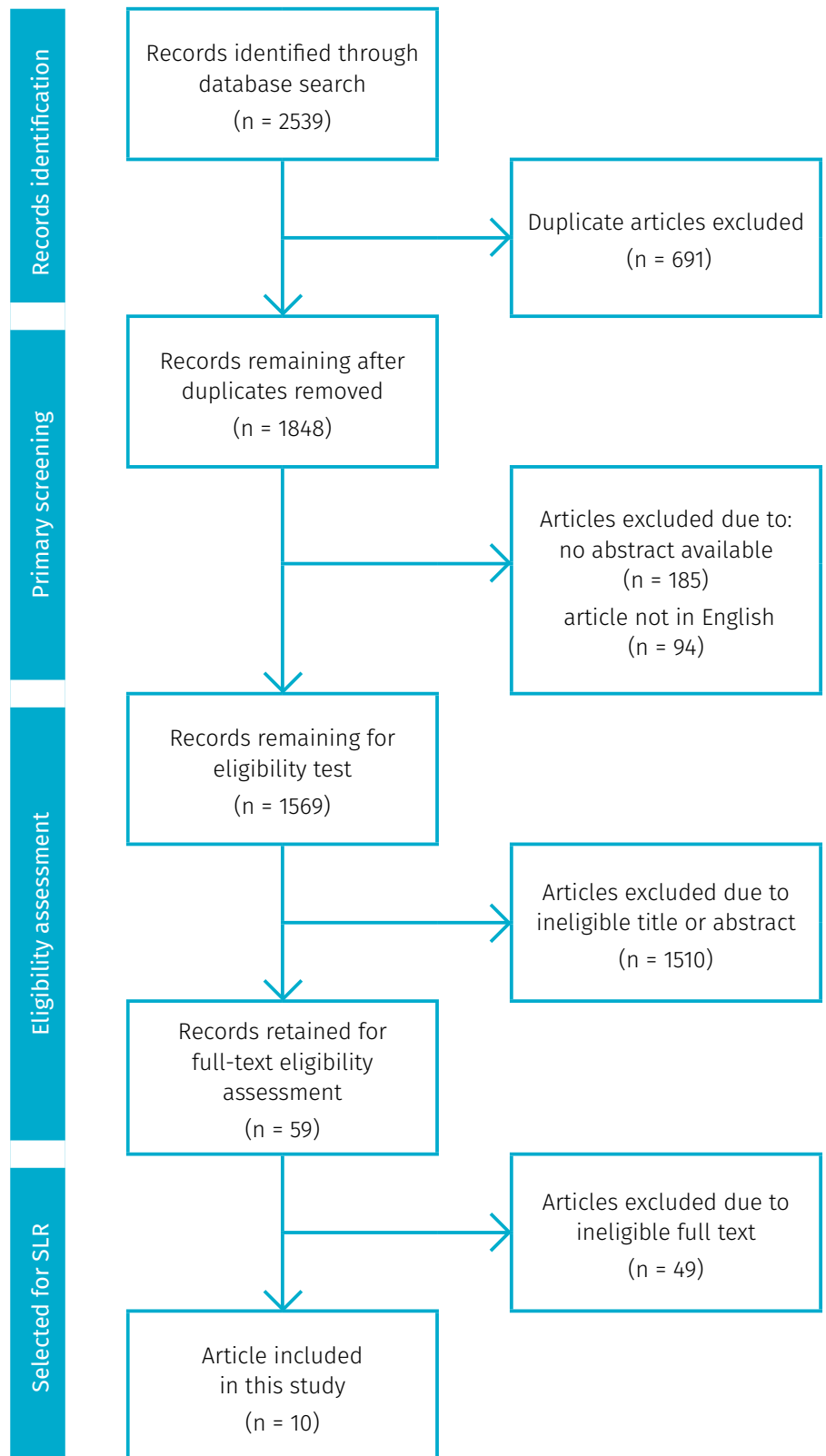
(MPM) did the primary extraction and selection and discussed these with KA and JG to resolve if any conflict arose. The final selected papers were shared and evaluated by KA and JG independently. One study was excluded at the last stage due to disagreement among the researchers. This procedure ensures selection reliability and reduces the risk of bias. For each of the ten finally selected articles, the authors, publication year, types of surgery, data collection period, places/settings/country, all hospitalisation costs, LOS, and currency were extracted.

### Quality appraisal

To ensure the quality of the selected studies and reduce the risk of bias, the Newcastle-Ottawa Quality Assessment Scale (NOS)<sup>37</sup> was used to assess the studies. The NOS is a well-established tool for cohort study evaluation in systematic reviews and meta-analyses. The NOS not only checks the study quality (i.e. study selection and comparability between the populations) but also measures the risk of bias in study outcomes or exposure variables. A score-based evaluation, with maximum NOS score of 9, was used to assess the risk of bias and indicate the study quality with 7 or higher indicating high quality, 5 or 6 indicating fair or moderate quality and less than 5 indicating high risk of bias.

### Cost values and currency conversion

The extracted cost information from the articles were in different currency values and over various time periods. To make an easy, presentable and scientific comparison, the cost data was converted by using a well-established conversion method, namely, purchasing power parity (PPP), using US dollars in 2020 as the conversion year for comparison purposes.<sup>38</sup>



**Figure 1: The PRISMA framework flowchart for this systematic literature review**

## Results

### Literature search outcomes

The search results were collected from the electronic databases using MeSH terms and POD-related keywords. The comprehensive literature search revealed a total of 2539 published records over the period from 2010 to 2020. The final selection strategies of the eligible studies are described in Figure 1 using the PRISMA framework. After excluding duplicates and articles with missing or non-English abstracts, 1569 studies continued to the next investigation step. Subsequently, these articles' titles and abstracts were screened considering the inclusion criteria and 1510 articles were excluded. Only 59 abstracts were found to fully or partly meet the inclusion criteria and the full texts of those articles were further assessed. Eleven articles were found to satisfy the inclusion criteria with one article excluded from the analysis after discussion with all researchers. Finally, ten full-text articles met the criteria and were selected for this review (see Figure 1).

### Characteristics of identified studies

All ten studies included cost information and the length of hospital stay for major surgery patients. Table 1 shows the basic characteristics of the included studies. The sample size of the selected studies varied from 66 to 1389526 for distinct major surgeries where the number of affected delirious patients ranged from 37 to 54615. The proportion of POD occurrence among patients varied widely from 0.8 to 78.5 per cent and these two extremes were for lumbar fusion (LF) or lumbar decompression

(LD) surgeries and respiratory failure or shock in surgical or medical ICU patients, respectively. Most of the studies were conducted in the USA (six studies),<sup>4,39–42,45</sup> two studies were conducted in South Korea<sup>43,44</sup> and one study from each of Australia<sup>22</sup> and Canada<sup>24</sup> (see Table 1).

Most of the selected studies were retrospective studies. They reported upon distinct types of major surgeries while one study<sup>22</sup> did not declare directly any particular surgery type. The studies only considered the medical or surgical acute inpatient, not their further treatment (if any) after discharge.

For the majority of post-operative patients, delirium was assessed by well-established methods, notably, confusion assessment method (CAM), confusion assessment method for the ICU (CAM-ICU), International Classification of Diseases (9<sup>th</sup> revision) Clinical modification (ICD-9-CM) codes and International Classification of Diseases and Related Health Problems (10<sup>th</sup> revision) Australian modification (ICD-10-AM) codes.

The NOS scores for the selected studies show minimal risk of bias and all but one study<sup>39</sup> had a score of seven or higher which indicates high quality (see supplementary material).

The age distribution of POD patients for the various major surgeries indicates that they were mostly elderly people of over 50 years. The mean age of POD and non-delirious patients varied from 49 to 87 years and 36 to 87 years, respectively. In two studies, the age distribution showed that POD also developed among young people under 40 years of age.<sup>4,40</sup>

The gender ratio of POD patients in seven studies showed that males

made up more than 50 per cent of patients. Overall, the proportion of males experiencing POD ranged from 29 to 84 per cent. A significant number of women had POD after the fragility hip fracture operation (82%) and lumbar fusion (LF) or lumbar decompression (LD) operations (55.5%).<sup>24,41</sup>

### Length of stay

The LOS after major surgeries was represented in two ways, namely, hospital stay and ICU stay (see Table 2). Seven studies reported inpatient LOS for hospital only, one study reported LOS for ICU only and two studies reported LOS for both hospital and ICU.

The LOS in most of the studies was represented using the mean and median along with variance/spread measurements, notably, interquartile range (IQR), standard deviation (SD) and range. Two studies reported only the mean LOS<sup>41</sup> and frequency distribution of LOS<sup>40</sup> without any other dispersion/variance measurements.

The day difference of LOS in hospital between POD and non-delirious patients ranged from 0.8 to 7.3 days (see Figure 2). The maximum mean LOS in hospital was found to be 20.2 days (SD ±13.6 days) for osteoporotic hip fractures surgeries for POD patients.<sup>44</sup> Median LOS in hospital was 7.0 days (IQR 4–11 days) for major urologic cancer surgeries.<sup>4</sup>

The LOS in ICU for delirious patients was reported in three studies and the lowest mean ICU stay was 54.4 hours (range 7–714 hours) and the highest median LOS was 75.6 hours (IQR 43.6–136.8 hours) for cardiac and major abdominal surgeries, respectively.<sup>42,43</sup>

**Table 1: Basic information about the included studies (n = 10)**

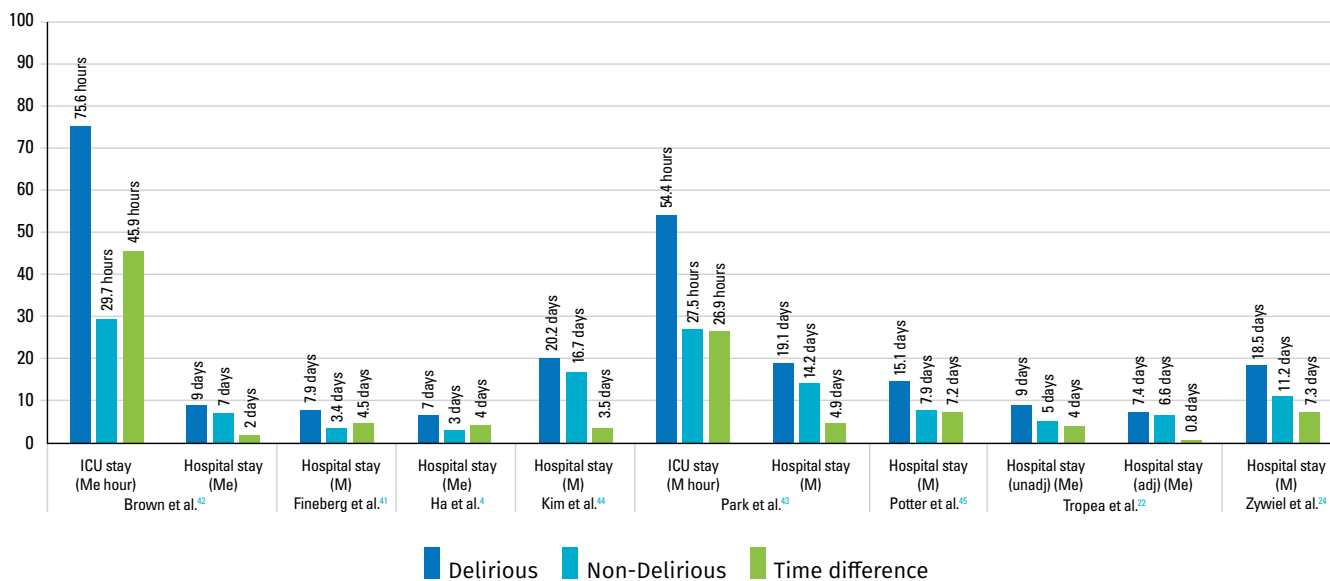
Author (year) Country	Type of surgery / medical facility used	Type of study	Sample size Total (delirious; per cent)	Time of data collection	Sex		Age (year) Mean (±SD or range)		Diagnostic tools for POD
					delirious	non-delirious	delirious	non-delirious	
Brown et al. (2016) <sup>12</sup> USA	cardiac surgery	Prospective observational study	N=66 (37; 56.1%)	October 2012 to February 2014	M: 28 (75.7%)	M: 23 (79.3%)	70 (±7)	69 (±8)	CAM/CAM- ICU
Fineberg et al. (2013) <sup>11</sup> USA	lumbar fusion (LF) or lumbar decompression (LD) surgeries	Retrospective database analysis	N=578 457 (4857; 0.8%)	2002 to 2009	F: 55.5%	F: 50.6%	70	55	ICD-9-CM
Ha et al. (2018) <sup>1</sup> USA	major urologic cancer surgeries – radical prostatectomy (RP), radical nephrectomy (RN), partial nephrectomy (PN) and radical cystectomy (RC)	Retrospective cohort study	RP: N=630 353 (5,986; 0.9%)	2003 to 2013	RP: M: 0.9%	RP: M: 99.1%	RP: 63.01	RP: 62.50	ICD-9-CM
			RN: N=305 503 (14 431; 4.7%) 291 072		RN: M: 60.6%	RN: M: 58.2%	RN: 72.12	RN: 64.27	
			PN: N=104,214 (3377; 3.2%)		PN: M: 59.1%	PN: M: 57.2%	PN: 67.01	PN: 61.00	
			RC: N=57,261 (6268; 10.9%)		RC: M: 84.3%	RC: M: 81.5%	RC: 74.04	RC: 70.07	
Kim et al. (2017) <sup>14</sup> South Korea	osteoporotic hip fractures	Follow-up study	N=221 (37; 16.7%)	2010 to 2014	M: 12 F: 25	M: 11 F: 26	81.8 (±6.8)	80.8 (±6.7)	CAM
Park et al. (2019) <sup>13</sup> South Korea	major abdominal surgery	Retrospective study	N=1061 (194; 19.1%)	January 2014 to December 2016	M: 126 (64.9%)	M: 567 (65.4%)	74.6 (60–91)	69.0 (60–95)	CAM
Patel et al. (2018) <sup>10</sup> USA	neuro-AIDS patient cohort	Cohort study	N=1 389 526 (54 615; 3.9%)	2005 to 2014	M: 70.06% F: 29.94%	M: 67.07% F: 32.93%	49	36	ICD-9-CM
Potter et al. (2018) <sup>15</sup> USA	transcatheter and surgical aortic valve replacement (TAVR and SAVR)	Retrospective study	TAVR: N=12 114 (195; 1.6%)	2015	TAVR: F: 5931 (48.96%)		TAVR: 87.06 (±3.77)		ICD-9-CM
			SAVR: N= 8974 (323; 3.6%)		SAVR: F: 3532 (39.36%)		SAVR: 84.20 (±2.67)		
Tropea et al. (2017) <sup>12</sup> Australia	medical or surgical acute inpatient	Retrospective cohort study	N=93 300 (6459; 6.9%)	July 2006 to June 2012	F: 3177 (49.2%)	F: 37 582 (43.3%)	80 (±9)	70 (±11)	ICD-10-AM
Vasilevskis et al. (2018) <sup>19</sup> USA	surgical or medical ICU for respiratory failure or shock	Prospective cohort study	N=479 (376; 78.5%)	2013	M: 248 (52%)		57 (±15)		CAM-ICU
Zywił et al. (2015) <sup>24</sup> Canada	fragility hip fracture		N=242 (126; 52.1%)	January 2011 to December 2012	M: 34 (29%) F: 82 (71%)	M: 40 (32%) F: 86 (68%)	85.3 (65- 103)	79.8 (65- 101)	CAM

CAM = Confusion Assessment Method; CAM-ICU = Confusion Assessment Method for the ICU; ICD-9-CM = International Classification of Diseases (9<sup>th</sup> revision) Clinical Modification codes; ICD-10-AM = International Classification of Diseases and Related Health Problems (10<sup>th</sup> revision) Australian Modification codes.

**Table 2: Length of stay (LOS) in hospital and/or ICU of delirious and non-delirious patients**

Author (year) Country	Type of surgery / medical facility used	Statistics	Length of stay in ICU and/or hospital		
				delirious (SD, IQR or range)	non-delirious (SD, IQR or range)
Brown et al. (2016) <sup>42</sup> USA	cardiac surgery	median (IQR)	ICU stay	75.6 hours (43.6–136.8)	29.7 hours (21.7–46.0)
			hospital stay	9 days (6–16)	7 days (5–8)
Fineberg et al. (2013) <sup>41</sup> USA	lumbar fusion (LF) or Lumbar decompression (LD) surgeries	mean	hospital stay	7.9 days	3.4 days
Ha et al. (2018) <sup>43</sup> USA	major urologic cancer surgeries	median (IQR)	hospital stay	7 days (4,11)	3 days (2,4)
Kim et al. (2017) <sup>44</sup> South Korea	osteoporotic hip fractures	mean (SD)	hospital stay	20.2 days (±13.6)	16.7 days (±6.9)
Park et al. (2019) <sup>43</sup> South Korea	major abdominal surgery	mean (range)	ICU stay	54.4 hours (7–714)	27.5 hours (8–460)
			hospital stay	19.1 days (5–60)	14.2 days (4–94)
Patel et al. (2018) <sup>40</sup> USA	neuro-AIDS patient cohort	frequencies	hospital stay		
			1–3 days	22.74%	35.89%
			4–6 days	24.20%	28.66%
			7–9 days	16.93%	14.21%
			10–12 days	9.81%	6.91%
			13–15 days	6.71%	4.48%
			≥ 16 days	19.60%	9.84%
Potter et al. (2018) <sup>45</sup> USA	transcatheter and surgical aortic valve replacement (TAVR and SAVR)	mean (CI)	hospital stay		
			for all AVR	15.1 days (12.0–18.0)	7.9 days (7.8–8.0)
			for TAVR	11.9 days (10.3–13.5)	6.1 days (6.0–6.2)
			for SAVR	17.0 days (12.2–21.7)	10.4 days (10.2–10.5)
Tropea et al. (2017) <sup>22</sup> Australia	medical or surgical acute inpatient	median (IQR)	hospital stay (unadjusted)	9 days (5–16)	5 days (2–8)
			hospital stay (adjusted)	7.4 days (6.7–10.0)	6.6 days (5.7–8.3)
Vasilevskis et al. (2018) <sup>38</sup> USA	surgical or medical ICU for respiratory failure or shock	median (IQR)	ICU stay	11 days (7–18)	
Zywiel et al. (2015) <sup>24</sup> Canada	fragility hip fracture	mean (range)	hospital stay	18.5 days (4–137)	11.2 days (3–107)





**Figure 2: Length of stay (LOS) in hospital and/or ICU for delirious and non-delirious patients**

M = mean; Me = median

Note: Patel et al. presented LOS as frequencies and Vasilevskis et al. did not compare LOS for delirious and non-delirious patients.

### Costs due to POD

Eight studies used the mean<sup>4,24,39-41,43-45</sup> and two studies showed median costs.<sup>22,42</sup> Studies also reported 95 per cent confidence interval (CI), IQR and SD. One study reported the standard error with the mean cost<sup>40</sup>. Interestingly, three studies did not report any variance measurement and only reported mean cost.<sup>4,41,43</sup>

Costs associated with POD after major surgeries and severe medical conditions were reported in several ways, notably, total or overall cost, hospitalisation and hospitalisation admission cost, index hospitalisation and admission cost and care cost (see Table 3).

There was a significant heterogeneity among the cost reporting for POD. Six studies reported 'total' or 'overall' cost<sup>39-44</sup> which indicated the total cost of hospitalisation without any breakup into direct or indirect treatment costs. Four studies also reported hospitalisation or hospital admission costs.<sup>4,40,44,45</sup> Two

studies reported the costs as index hospitalisation and index admission cost<sup>22,45</sup> and one study represented the costs as care cost<sup>21</sup>.

The overall cost for POD patients ranged from median US\$7396 (IQR US\$3250 – US\$15,005)<sup>22</sup> up to US\$57306 (IQR: US\$48718 – US\$88759)<sup>42</sup> for medical or surgical acute inpatient and cardiac surgery, respectively. The mean hospitalisation cost and hospital admission cost varied from US\$8558 (SD US\$3260.78) to US\$20940 (SE ± US\$483.40) for osteoporotic hip fractures and neuro-AIDS patient cohorts.

Two studies conducted in Australia<sup>22</sup> and the USA<sup>45</sup> reported index hospitalisation costs and the index admission costs coded for medical or surgical acute inpatient and the trans-catheter and surgical aortic valve replacement surgeries, respectively. The unadjusted mean index hospitalisation cost for POD patients was reported as US\$82403 (95% CI US\$70816 – US\$93991) and

median index admission cost as US\$13167 (IQR US\$10512 – US\$17299).

One study examined hip fracture surgeries<sup>24</sup> and reported mean care cost for POD patients as US\$24416 (IQR US\$8141 – US\$10945). Another study<sup>39</sup> reported costs for POD as total cost and its components – pharmacy; laboratory; diagnostic radiology; respiratory, physical therapy and occupational therapy; central supply; professional, bed expenses and dialysis. That study reported that the total 30-days cumulative incremental cost due to POD was US\$20105 (95% CI US\$12547 – US\$26484) and the incremental cost effect of mortality was US\$5245 (95% CI US\$2317 – US\$8869) for surgical or medical ICU patients suffering from respiratory failure or shock.<sup>39</sup>

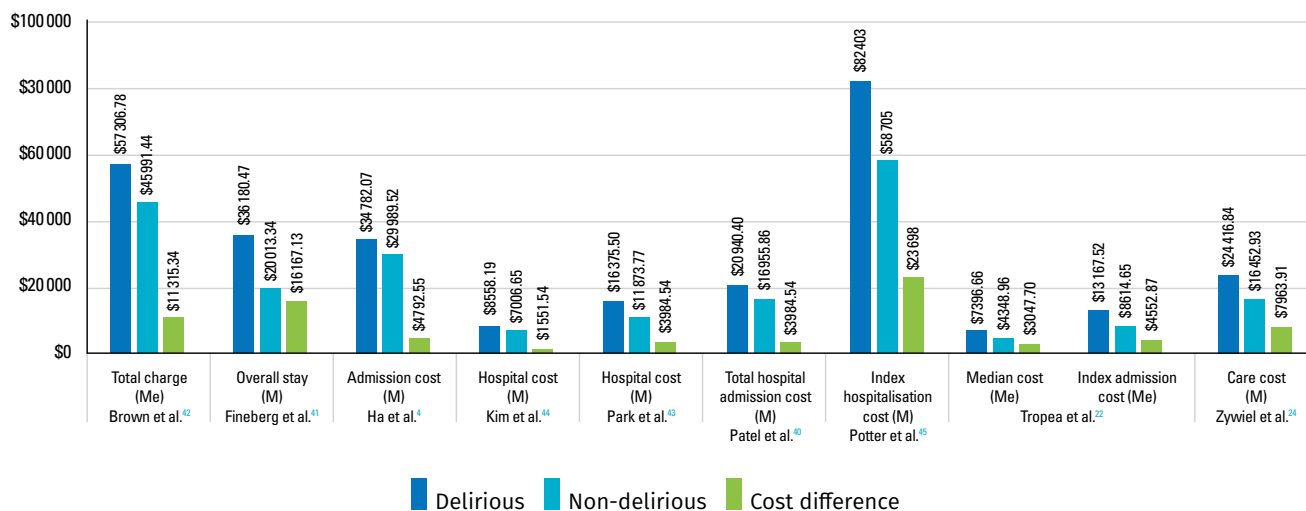
The cost differences between POD and non-delirious patients ranged from US\$1551 to US\$23698 (see Figure 3) for osteoporotic hip fracture surgery<sup>44</sup> and transcatheter and surgical aortic valve replacement surgeries,<sup>45</sup> respectively.

**Table 3: Cost data for delirious and non-delirious patients (n = 10)**

Authors (year)	Year of cost data	Currency	Statistics	Outcome measures	Original costs	PPP 2020 USD values
Brown et al. (2016) <sup>42</sup>	October 2012 to February 2014	USD	Median (IQR)	Overall charges	45 459 (36 607–67 807)	50 286.83 (40 494.73–75 008.22)
				Total charges with delirium	51 805 (44 041–80 238)	57 306.78 (48 718.23–88 759.42)
				Total charges without delirium	41 576 (35 748–43 660)	45 991.44 (39 544.5–48 296.77)
Fineberg et al. (2013) <sup>41</sup>	2002 to 2009	USD	Mean	Overall cost with delirium	29 970	36 180.47
				Overall cost without delirium	16 578	20 013.34
Ha et al. (2018) <sup>43</sup>	2003 to 2013	USD	Mean	Admission cost with delirium	30 859	34 782.07
				Admission cost without delirium	26 607	29 989.52
Kim et al. (2017) <sup>44</sup>	2010 and 2014	USD	Mean (IQR) Mean (SD)	Overall hospitalisation cost	6973 (3924–17 222)	7713.99 (4340.74–19051.01)
				Hospitalisation cost with delirium	7736 (2947.73)	8558.19 (3260.78)
				Hospitalisation cost without delirium	6333 (1698.24)	7006.65 (1878.6)
Park et al. (2019) <sup>45</sup>	January 2014 to December 2016	KRW (x10 <sup>3</sup> )	Mean (range)	Hospital costs with delirium	12 816 (755–73 168)	16 375.50 (964.69–93 489.57)
				Hospital costs without delirium	9292 (498–75 270)	11 873.77 (636.31–96 175.38)
Patel et al. (2018) <sup>46</sup>	2005 to 2014	USD	Mean ± SE	Total cost of hospital admission for patients with HIV-associated cognitive impairment	18 930 ± 436.99	20 940.4±483.40
				Total cost of hospital admission for patients without HIV-associated cognitive impairment	15 328 ± 216.97	16 955.86±240.01
Potter et al. (2018) <sup>45</sup>	2015	USD	Mean (95% CI)	Unadjusted index hospitalisation cost with delirium	82 403 (70 816–93 991)	90 189.64 (77 507.73–102 872.65)
				Unadjusted index hospitalisation cost without delirium	58 705 (58 294–59 116)	64 252.31 (63 802.47–64 702.15)
Tropea et al. (2017) <sup>42</sup>	1 July 2006 to 30 June 2012	AUD	Median (IQR)	Unadjusted median cost with delirium	9504 (4176–19 280)	7396.66 (3250.05–15 005.01)
				Adjusted median cost with delirium	15 640 (12 678–21 096)	12 172.12 (9866.89–16 418.35)
				Unadjusted median cost without delirium	5588 (2661–12 256)	4348.96 (2070.97–9538.46)
				Adjusted median cost without delirium	10 422 (8927–12 946)	8111.11 (6947.6–10 075.46)
				Cost of the index admission with delirium	16 919 (13 507–22 228)	13 167.52 (10 512.07–17 299.35)
				Cost of the index admission without delirium	11 069 (9677–14 068)	8614.65 (7531.3–10 948.68)

Authors (year)	Year of cost data	Currency	Statistics	Outcome measures	Original costs	PPP 2020 USD values	
Vasilevskis et al. (2018) <sup>39</sup>	2013	USD	Mean (95% CI)	<i>Estimates of the 30-day cumulative incremental effects of ICU delirium</i>			
				<i>Incremental cost attributed to intensity of utilisation:</i>	Total cost	17 838 (11 132–23 497)	20 105.73 (12 547.20–26 484.15)
					Pharmacy	4 018 (2582–5020)	4528.80 (2910.25–5658.19)
					Laboratory	1185 (539–2047)	1335.65 (607.52–2307.23)
					Diagnostic radiology	665 (373–1028)	49.54 (420.42–1158.69)
					Respiratory, physical therapy and occupational therapy	904 (520–1339)	1019.26 (586.11–1509.23)
					Central supply	2434 (1592–3229)	2743.43 (1794.39–3639.50)
					Professional, bed expenses and dialysis	13 965 (8698–19457)	15 740.35 (9803.77–21 930.55)
				<i>Incremental cost attributed to mortality:</i>	Total cost	4654 (2056–7869)	5245.66 (2317.38–8869.38)
					Pharmacy	843 (334–1396)	950.17 (376.46–1573.47)
					Laboratory	270 (14–604)	304.32 (15.78–680.79)
					Diagnostic radiology	142 (45–244)	160.05 (50.72–275.02)
					Respiratory, physical therapy and occupational therapy	324 (138–536)	365.19 (155.54–604.14)
					Central supply	399 (-47–766)	449.72 (-52.98–863.38)
Professional, bed expenses and dialysis	4564 (1666–7872)	5144.22 (1877.80–8872.76)					
Zywiel et al. (2015) <sup>34</sup>	January 2011 to December 2012	CAD	Mean (IQR)	Care cost with delirium	26 272 (8760–117 769)	24 416.84 (8141.42–109 452.91)	
				Care cost without delirium	17 703 (5113–122 246)	16 452.93 (4751.95–113 613.77)	

PPP = purchasing power parity; AUD = Australian dollar; CAD = Canadian dollar; KRW = Korean won; USD = US dollar; CI = confidence interval; IQR = interquartile range; SD = standard deviation; SE = standard Error



**Figure 3: Cost comparison (PPP values, in US\$) for delirious and non-delirious patients**

M = mean; Me = median

Note: Vasilevskis et al. did not compare costs for delirious and non-delirious patients.

## Discussion

In this systematic review a total of ten studies that met the inclusion criteria were reviewed. These studies had information about the extra LOS in hospital and ICU after major surgery and the associated hospital costs for an episode of POD. The studies reported the incidence of POD varied widely from 0.8 to 78.5 per cent which, in part, is explained by different study settings, study population characteristics, types of surgeries as well as the delirium diagnostic methods used after surgery. The delirium assessment method employed to identify POD might also have an impact on the extent of diagnosis of POD. The studies which used CAM as a POD diagnostic tool had greater numbers of delirious cases (16.7 to 78.5 per cent) compared to other methods like ICD-9-CM codes and ICD-10-AM codes (0.8 to 10.9 per cent). These outcomes demand a deeper investigation of POD assessment methods.

Age has been identified as a predominant factor for the occurrence of POD.<sup>46,47</sup> An age of 70

years or more is a well-recognised risk factor for POD which influences post-operative comorbidities and recovery.<sup>47-52</sup> It was observed that the older patients were the more likely they were to experience POD. Most studies reported on patient groups older than 70 years. Conversely, Patel<sup>40</sup> reported that a significant number of young neuro-AIDS patients (<44 years) also experienced POD (~31%). It was also observed in five studies<sup>6,22,40,42,43</sup>, that male patients were more affected by POD than female patients. Therefore, gender specific interventions for aged people who undergo major surgery should be undertaken to minimise the risk of POD.

All the costs reported in the studies were found to be significantly higher in POD patients compared to those who were not delirious. Kim,<sup>44</sup> in Korea, reported the lowest cost difference between delirious and non-delirious patients at US\$1551.54. Potter et al.,<sup>45</sup> in their USA study, reported the highest cost difference between the groups at US\$23 698 which is significantly higher than in other countries and for other types of surgeries. Also, the six USA

studies exhibited significant cost variation ranging from US\$3984 to US\$23 698<sup>45</sup> for different types of surgeries and hospital settings. The reported hospitalisation cost for POD of hip fracture surgeries in Canada<sup>24</sup> suggested that the cost is higher there than in Asia and Australia. A single study conducted in Australia<sup>22</sup> reported that delirious patients cost US\$3047 extra compared to the non-delirious patient, which is lower than the USA and Canada but about two times higher than Korea.

The study results show that POD significantly increased the costs of procedures and recovery in all clinical settings and in all surveyed countries by an average of US\$8105. Comparatively, the costs were lower in Asia and higher in the USA with Canadian and Australian costs in between. Unlike other studies, Vasilevskis<sup>39</sup> reported a comprehensive distribution of the incremental costs regarding the intensity of utilisation and mortality for the ICU delirious versus non-delirious patients. The study showed that the 30-day cumulative incremental cost due to POD was significantly higher

than for non-delirious patients and the incremental cost attributed to intensity of utilisation is higher than that attributed to mortality, for all cost classes.

The LOS in hospital and/or ICU was investigated for all the selected studies and it was found that delirious patients needed to stay more days in hospital and more hours in ICU than other patients. The maximum days of hospital stay for delirious patients was 20.2 days after osteoporotic hip fractures surgery in Korea,<sup>44</sup> followed by 19.1 days after major abdominal surgery in the USA<sup>43</sup> and 18.5 days after hip fracture surgery in Canada.<sup>24</sup> Although the costs reported by Korean studies were lower than in other countries, the LOS in hospital was higher in many instances. The greatest difference in LOS was reported by Zywił et al. in patients who experienced POD after hip fracture surgery – on average POD patients stayed 7.3 days longer than non-delirious patients.<sup>24</sup> However, this study considered older patients than the other studies and this may be a reason for longer stays in hospital after surgery. Tropea<sup>22</sup> reported the lowest LOS day difference between delirious and non-delirious medical or surgical acute inpatients, while Vasilevskis<sup>39</sup> reported the median LOS in ICU for surgical or medical ICU patients for respiratory failure or shock was 11 days (IQR 7–18 days) for the both delirious and non-delirious patients. Patel<sup>40</sup> presented the distribution of the hospital stay after surgery for neuro-AIDS patients – 22.74 per cent of delirious patients stayed one to three days compared to 35.89 per cent of non-delirious patients, 24.20 per cent of delirious patients stayed four to six days compared to 28.66 per cent of non-delirious patients, and 53.05 per cent of delirious patients

stayed seven days or longer compared to 35.44 per cent of non-delirious patients. The other studies also showed significant differences in LOS between the delirious and the non-delirious cohorts. Regarding LOS in ICU, studies in the USA reported that LOS in ICU after major abdominal surgery was 26.9 hours longer for POD patients than non-delirious patients<sup>43</sup> and after cardiac surgery was 45.9 hours longer for POD patients than non-delirious patients.<sup>42</sup> Four studies were conducted in the USA in same year, 2018, and reported distinct costs and LOS for different surgeries.

All studies reflected that LOS in hospital after major surgery was increased for POD patients compared to non-delirious patients.

### Study limitations

First, the studies were selected from the PubMed and MEDLINE databases only. The number of studies might increase if other databases had been explored. Secondly, the timeframe for searching the studies covered only the past ten years (2010–2020) which might be a limitation to finding more studies based on the inclusion criteria. The results show that most of the studies were conducted very recently (i.e. 2017–2019) and were mainly (six out of ten) from the USA. A few studies were conducted in Asia and Australia and no studies were found from Europe and Africa. Finally, most of the studies adopted a retrospective study setup and considered the costs and LOS data from 2002 to the most recent year 2016. Furthermore, only peer-reviewed and publicly available English articles were considered. This study only focused on the cost and LOS due to POD, therefore further in-depth investigation of other factors associated with POD will be informative.

## Conclusions

This systemic review revealed ten studies captured the cost burden and LOS in hospital and ICU for surgical patients who developed POD. The selected studies were conducted mostly in the USA with two in South Korea and single studies in Australia and Canada. Surprisingly, no Europe studies were sighted. The present review clearly identified and summarised that hospital costs and LOS significantly increase due to POD. Although the cost increment/quantum because of POD was lower in Asia, it was extremely high in the USA studies. The highest cost due to POD was reported for the trans-catheter and surgical aortic valve replacement in USA and lowest cost in South Korea for osteoporotic hip fractures. Further clinical investigations are needed to decipher the detailed and distinct cost drivers related to POD. The present findings clearly indicate that total costs of treatment are increased with the occurrence of POD after major surgeries. This review also suggests that a gender specific investigation could be warranted as well as a deeper investigation of POD assessment methods. The outcomes of this review should be helpful for policy development regarding the different health care settings and specific cost drivers aimed at diminishing the overall costs of POD and the risk of its occurrence in surgical and hospital settings.

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