The economic impact of delirium in Australia in 2016-17: a cost of illness study

Additional File 1. Supplementary methods

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1 CHEERS checklist

CHEERS checklist

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Page 1, line 3.
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Page 2, line 1-26.
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	Page 4, line 43-74.
		Present the study question and its relevance for health policy or practice decisions.	Page 5, line 71-81.
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 6, line 102-104.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 6, line 94-101.
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 6, line 92-93.
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Not applicable. No interventions or strategies are compared.
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 6, line 92-93.
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 12, line 236-238.
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, line 94-101.
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Not applicable. No interventions are considered.
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Not applicable. No interventions are considered.
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable. No interventions are considered.
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 9, line 161-248.
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable.

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Section/item	Item No	Recommendation	Reported on page No/ line No
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 7, line 169-248. Page 13, line 256-259.
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Not applicable for cost of illness studies.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Not applicable for cost of illness studies.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 5, line 82-248.
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Page 5, line 82-248.
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Not applicable for cost of illness studies.
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Page 19, line 352-361.
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Not applicable for cost of illness studies.
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Not applicable.
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Page 20, line 362-431.
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 25, line 454.
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 24, line 452.

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2 Literature review strategy

A targeted rather than systematic literature review was performed to identify relevant articles with the purpose of identifying the prevalence of delirium within hospital settings and in residential aged care facilities, the duration of delirium, and mortality due to delirium. The review also identified literature relevant to costs of delirium, including health system, productivity, and wellbeing impacts. Keywords were restricted to the title and abstract for searches conducted on PubMed.

1. ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]) AND Meta-Analysis[ptyp].
2. ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]) AND "Australia"[pl].
3. ("epidemiology"[MH] OR "mortality"[MH] OR "incidence"[MH] OR "prevalence"[MH] OR “duration”[tiab] OR “persistence”[tiab]) AND ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab])).
4. 3 AND "Australia"[pl].
5. 3 AND "Australia"[pl] AND (“hospital”[tiab] OR “aged care”[tiab] OR “nursing home”[tiab]).
6. ("cost"[tiab] OR "economic"[tiab] OR "productivity"[tiab] OR "workforce"[tiab] OR “health use”[tiab] OR “utilization”[tiab]) AND ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]).
7. 5 and "Australia"[pl].
8. ("burden"[tiab] OR "disability"[tiab] OR "death"[tiab] OR “quality of life”[tiab]) AND ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]).
9. 7 AND "Australia"[pl].

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3 Epidemiology

A targeted rather than systematic literature review was performed to identify relevant articles with the purpose of identifying the prevalence of delirium within hospital settings and in residential aged care facilities, the duration of delirium, and mortality due to delirium.

3.1 Prevalence in episodes of acute hospital care

Results from the literature search were pooled to estimate an average prevalence that can be applied to Australian hospital separations[a]. The studies, characteristics and pooled results are shown in Table 1. Studies were pooled using weights based on the sample size.

Table 1: Occurrence rates of delirium

Author, year	Country	Sample restrictions	Sample size	Mean age (SD)	Assessment frequency	Occurrence/ prevalence (%)
Sources cited in Siddiqi et al[4]						
Braekhus 1994	Norway	> 75 years	58	83.1	Every 3 days	24.1
Cameron 1987	US	No age restriction	133	68.8	On request	15.0
Feldman 1999	Israel	>70 years, admissions to geriatric unit	61	83.2 (6.8)	Every 2 days for 14 days, intermittently until discharge or death	18.0
Jitapunkul 1992	UK	Admissions to geriatric unit	184	81.7 (6.6)	At admission, 1 week, discharge and case record review	21.7
Johnson 1990	US	>70 years	235	78 (6.0)	Within 24 hours and every day	20.4
O'Keefe 1996	Ireland	No age restriction	225	82 (4.0)	Within 24 hours and every 2 days	41.8
Rockwood 1989	Canada	Elderly	80	76.8	Daily	25.0
Rockwood 1993	Canada	Admissions to geriatric unit	168	79 (8.0)	At admission, timing not clear	25.6
Seymour 1980	Canada	>70 years	68	81.2	Within 4 hours, weekly	16.2
Zanocchi 1998	Italy	Admissions to geriatric unit	585	77.1	Twice-daily	22.2
Total/weighted average			1,797	80.3 (4.4)		24.0
Recent point-prevalence/occurrence studies						
McAvay, 2006[7]	US	>70 years	433	79.8 (6.3)	Daily	12.7
Holden, 2008[8]	New Zealand	>65 years	216	79.3	Every 2 days until discharge	29.1

[a] Three studies from Siddiqi et al[4] were removed from the analysis. Two of the studies were restricted to a sample of patients who were admitted from community dwellings),[5;6] while one study was removed because there were insufficient details to assess the methods were appropriate as the full text article was not available in English.[7]

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Author, year	Country	Sample restrictions	Sample size	Mean age (SD)	Assessment frequency	Occurrence/ prevalence (%)
McCusker, 2003[9]	Canada	>65 years	1,552	83.6 (7.4)	-	22.3
Inouye, 1998[10]	US	>65 years, medical and surgical patients	107	-	Admission and discharge	25.0
Jones, 2006[11]	US	>70 years	491	79.0 (6.0)	Daily	22.0
Inouye, 1998[10]	US	>65 years, medical and surgical patients	174	-	Admission and discharge	15.0
Ryan 2013[12]	Ireland	Adults, no restriction	280		Point prevalence	17.6
Bellelli 2016[3]	Italy	>65 years	1,867	82 (7.4)	Point prevalence	22.9
Meagher 2014[13]	Ireland	Adults, no restriction	311	76 (13.1)	Point prevalence	16.7
Iseli 2007[14]	Australia	>65 years	104	80.1 (7.0)	At admission, follow up at 2-3 days, and then weekly	21.0
Travers 2013[15]	Australia	>70 years	493	80.4 (6.5)	Daily	17.3
Speed 2007[16]	Australia	Adults, no restriction	1,209	80.0	Four point prevalence audits	10.9
Total/weighted average			7,237	81.1 (7.4)		19.2
Overall			**9,034**	**80.9 (6.6)**		**20.2**

Source: Based on Siddiqi et al[4] and sources as itemised in the table. Weighted averages are based on sample size.

3.2 Duration of delirium episodes

As delirium is a transient condition, it is important to estimate the average duration of an episode of delirium to calculate the burden imposed on society (Table 2).

Table 2: Duration of delirium

Author, year	Country	Sample restrictions	Sample size	Age (SD)	Duration (days)
Adamis, 2006[24]	England	Elderly care unit;≥70 years	94	82.8 (6.5)	8.6
Andrew, 2005[25]	Canada	Admissions to geriatric unit	77	78.5 (7.2)	6.3
O'Keeffe, 1997[26]	Ireland	Admissions to geriatric unit	94	83.2 (6.8)	7.0
Pandharipande, 2013[27]	US	Admissions to intensive care unit (ICU) with defined list of conditions; excluded those with recent ICU exposure	606	61	4.0
Rockwood, 1993[28]	Canada	Admissions to geriatric unit, mostly admitted from community	173	79 (8)	8.0
Van den Boogaard, 2012[29]	Netherlands	Admissions to ICU; excluded those admitted for < 1 day	272	81.7 (6.6)	2.0
Cole, 2012[30]	Canada	Long-term care residents	279	87.4	11.3
Total/weighted average			**1,595**		**5.9**

Source: sources as itemised in the table. The weighted averages were based on sample size.

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3.3 Mortality associated with delirium

Delirium is associated with higher rates of mortality in hospital settings, and a greater chance of mortality occurring in the year following an episode of delirium. Mortality was estimated using an attributable fraction approach based on literature. Witlox et al[31] reported an overall average mortality rate of 38.0% compared to a rate of 27.5% with no delirium, which was a 1.4-fold increase for those with delirium. The hazard ratio – indicating how much more likely someone with delirium is to have died at any point in time – was estimated to be 1.95. The authors included seven studies from the US, UK, Canada, Chile and Brazil. To estimate mortality associated with delirium for Australia, the Chilean and Brazilian studies have been excluded from the analysis as they are demographically less similar to Australia and there may be alternative drivers of mortality in those countries. The hazard ratio was re-estimated by meta-analysis using a random effects model. The final reweighted hazard ratio was estimated to be 1.77 (Table 3).

Table 3: Mortality rates and hazard ratio for mortality

Author, year (as cited in Witlox et al[31])	Country	Subgroup	Hazard ratio for mortality (95% confidence interval)
Gonzalez et al 2009	Chile	General medical	4.04 (2.19 – 7.46)
Furlaneto and Garcez-Leme 2007	Brazil	Femoral fracture	1.28 (0.66 – 2.48)
Leslie et al 2005	US	General medical	1.62 (1.13 – 2.33)
McCusker et al, 2002	Canada	General medical	2.16 (1.06 – 4.41)
Nightingale et al, 2001	UK	Hip fracture	2.40 (1.66 – 3.48)
Rockwood et al, 1999	Canada	General medical	1.80 (1.11 – 2.92)
Francis and Kapoor, 1992	US	General medical	1.40 (0.79 – 2.48)
Pooled estimate			**1.95 (1.51 – 2.52)**
Reweighted estimate			**1.77 (1.39 – 2.15)**

Source: Based on Witlox et al[31]

The hazard ratio (1.77) based on data from Witlox et al[31] was applied to general population mortality rates, including the 1.4-fold increase for mortality for people who had delirium, for the respective age groups to estimate the number of deaths associated with delirium in 2016-17. It was expected that 12,571 people who had delirium would die in 2016-17, noting not all mortality is due to delirium itself (e.g. comorbid dementia or other illness may contribute to both delirium and death). Deaths

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due to delirium were estimated by applying the population attributable fraction to total deaths in the delirium cohort in 2016-17.[b]

[b] The formula to estimate the number of deaths attributable to delirium is as follows:
$Population\ attributable\ fraction = \frac{P.(HR-1)}{P.(HR-1)+1}$, where P equals the prevalence rate for each age group, and HR equals the hazard ratio. The population attributable fraction is then multiplied by the total number of deaths that occur in people with delirium.

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4 Hospital expenditure

Hospital expenditure data in Australia includes general public and private hospital admissions. The literature shows that delirium results in functional decline, resulting in a longer length of stay (LOS) for hospital patients, consequently leading to higher hospitalisation expenditure.

To establish the incremental change in LOS for hospital patients with delirium, a targeted review of the relevant literature was conducted for studies that are demographically similar to Australia and that assessed outcomes for patients admitted to general medical wards.

The results of these studies were weighted by sample size to estimate the additional LOS for people with delirium. On average, the LOS for people with delirium was estimated to be 24.2 days rather than 16.7 days in the control groups, a difference of 7.5 days (Table 4). Additional studies were used to estimate the proportion of additional days that are due to delirium after controlling for confounding factors. When additional factors are controlled for, including the baseline characteristics of patients, delirium accounts for 36% of the additional days, as shown in Table 5. As such, we estimate that delirium increases the average LOS by 2.7 days.

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Table 4: Additional LOS associated with delirium

Author, year	Country	Sample characteristics	Sample size	Difference in LOS
Alexander, 2016[32]	UK	Admissions to general hospital	590	6.0
Emond, 2017[33]	Canada	Admissions to ICU; ≥ 65 years	200	8.6
Gaudet, 1993[34]	France	Admissions to geriatric unit	487	18.0
Jitapunkul, 1992[35]	UK	Admissions to acute geriatric ward; ≥60 years	184	4.0
Kolbeinsson, 1993[36]	Iceland	Admissions to emergency ward; ≥70 years	272	2.9
McCusker, 2003[37]	Canada	Acute care; ≥65 years	359	3.6
O'Keeffe, 1997[26]	Ireland	Admissions to geriatric unit	225	10.0
Ramsay, 1991[38]	UK	Admissions to acute geriatric ward	119	-1.9
Rockwood, 1993[28]	Canada	Admissions to geriatric unit	173	4.0
Stevens, 1998[39]	Australia	Admissions to general medical	84	12
Tan, 2015[40]	New Zealand	>65 years	250	3.8
Thomas, 1988[41]	US	Admissions to general medical ward	133	11.0
Total / weighted average			**3,076**	**7.5**

Source: as itemised in table.

Table 5: Adjusted and unadjusted difference in LOS due to delirium

Author, year	Country	Sample characteristics	Sample size	Unadjusted difference	Adjusted difference	Relativity
Emond, 2017[33]	Canada	Admissions to ICU; ≥ 65 years	200	8.6	8.4	0.98
Inouye, 1998[10]	US	≥65 years	727	1.2	0.5	0.42
McCusker, 2003[37]	Canada	Acute care; ≥65 years	359	4.5	0.5	0.10
O'Keeffe, 1997[26]	Ireland	Admissions to geriatric unit	225	10.0	0.7	0.07
Total / weighted average			**1,511**	**4.3**	**1.5**	**0.36**

Source: as itemised in table.

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5 Informal care costs

Carers are people who provide care to others in need of assistance or support. An informal carer provides this service without formal payment and does so outside of the formal care sector. An informal carer will typically be a family member or friend of the person receiving care, and usually lives in the same household as the recipient of care.

Bellelli et al[55] found that 26.2% of patients who developed delirium during their hospital stay required assistance from paid caregivers following discharge. The rate of paid caregiving was assumed to be comparable to informal care in Australia as the care is usually provided by family members. In order to estimate the number of care recipients for Australia, 26.2% was applied to the prevalence of delirium for people who are 65 years or older and who live in the community (total adjusted prevalence – prevalence in aged care). Therefore, it was estimated that 20,741 people would require care due to delirium in Australia in 2016-17. People with delirium required assistance with an additional 0.36 activities of daily living over a period of 12 months.[56,57]

Analysis of the Survey of Disability, Ageing and Carers,[58] revealed an almost linear trend, such that an additional 2.57 hours of care were provided per week for each additional activity on average.[c] As such, each person would receive 0.9 additional hours of care per week or 47.6 hours of care throughout the year.

The carer's opportunity cost of time was calculated based on the weighted average weekly earnings[54] and the chance of being employed.[53]

[c] Care needs would likely depend on the type of activity for which help is required; however there was insufficient evidence to determine which activities are most influenced by delirium.

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6 References

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