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

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ABSTRACT

Objectives: To estimate the economic impact of delirium in the Australian population in 2016-17, including financial costs, and its burden on health.

Design, Setting and Participants: A cost-of-illness study was conducted for the Australian population in the 2016-17 financial year. The total cost of delirium was estimated using standard cost-of-illness methodology. The prevalence of delirium in 2016-17 was calculated to inform cost estimations.

Main outcome measures: The total and per capita costs were analyzed for three categories: health systems costs, other financial costs including productivity losses and informal care, and cost associated with loss of wellbeing (burden of disease). Costs were expressed in 2016-17 pound sterling (£) and Australian dollars (AUD).

Results: There were more than 132,000 occurrences of delirium in 2016-17, and more than 900 deaths were attributed to delirium in 2016-17. The total costs of delirium in Australia were estimated to be £4.3 billion (AUD8.8 billion) in 2016-17, ranging between £2.6 billion (AUD5.3 billion) and £5.9 billion (AUD12.1 billion). The total costs comprised financial costs of £1.7 billion and the value of healthy life lost of £2.5 billion.

Conclusions: These findings highlight the substantial burden that delirium imposes on Australian society-both in terms of financial costs associated with health system expenditure and the increased need for residential aged care due to the functional and cognitive decline associated with delirium and dementia. To reduce the substantial wellbeing costs of delirium, further research should seek to better

understand the potential pathways from an episode of delirium to subsequent mortality and reduced cognitive functioning outcomes.

Strengths and limitations of this study

- This study uses cost of illness methodology to estimate the total annual financial and wellbeing impacts of delirium for the first time in Australia.
- This study also estimates the costs of dementia that are associated with delirium in Australia, with significant implications for other high income western countries.
- This study is based on non-systematic search strategy to find relevant cost inputs, noting that a number of inputs are sourced from official Australian Government statistics.
- There were a number of data gaps when estimating costs, meaning the results of our study are only indicative of the total cost.
- Cost of illness studies provide guidance on the size of the problem, but more work is need to identify cost effective interventions to reduce the burden of delirium.

INTRODUCTION

Delirium is a common, serious, and often-fatal medical condition, characterized by an acute decline in cognitive functioning.[1] The term delirium is used to describe a transient, reversible neuropsychiatric syndrome that is of acute (abrupt or sudden) onset, with a fluctuating course which occurs in the setting of a medical condition. Acute confusion or impaired cognition are other terms that are commonly used to refer to delirium.[2]

The development of delirium has been associated with increased morbidity, persistent functional decline, increased nursing time per patient, higher hospital costs, higher rates of residential aged care placement and increased mortality.[2-4] It is also a significant risk factor for later onset of dementia and acceleration of cognitive decline.[3] Though underdiagnosed, it is highly prevalent in hospitalizations, particularly so for palliative care populations[5, 6]; as many as 50% of people over the age of 65 who are admitted to hospital experience delirium depending on the clinical setting.[2] Despite being preventable in more than a third of cases delirium remains the most common complication in hospitals today.[7]

A previous study in the United States, undertaken over a decade ago, assessed the costs associated with delirium after adjusting for patient sociodemographic and clinical characteristics and found that hospital costs per day for patients with delirium were more than double the costs of patients who did not experience an episode of delirium.[8] Additionally, previous studies have found associations between delirium and long-term cognitive impairment and dementia,[9] and

premature death.[3, 10] However, the relative costs of these outcomes have not yet been established.

To date, no studies have estimated the costs of delirium in Australia. Understanding the costs of delirium is important because it is difficult to diagnose. There are no diagnostic blood tests, x-rays or scans and hence it is often missed in as many as two thirds of cases.[11] By better understanding the costs of delirium, it is possible to answer the question of whether it would be worthwhile to pay more attention to its prevention, diagnosis and treatment.

Financial costs of delirium to the Australian health system include the costs of running hospitals and nursing homes, GP and specialist services reimbursed through Australia's universal health insurance scheme and private funds, the cost of pharmaceuticals and over-the-counter medications, allied health services, research and health administration. Other financial costs of delirium include productivity costs, the cost of informal care, funeral costs, and deadweight loss of taxation payments and administration. The burden of disease associated with delirium measures pain, suffering, and premature mortality in terms of disability adjusted life years (DALYs). Different costs of disease are borne by different individuals or sectors of society. Understanding how the costs are shared helps to make informed decisions regarding interventions.

The purpose of this study was to raise awareness of the impacts of delirium and contribute to improving policy in this area, by quantifying the magnitude of the

economic burden associated with delirium in Australia in 2016-17 on the basis of cost-of-illness methodology.

METHODS

Prevalence

This study was conducted using standard cost-of-illness methodology,[12] based on a prevalence approach to cost measurement. Prevalence approaches measure the number of people with a given condition in a base period and the costs associated with treating them, as well as other financial and non-financial costs in that year due to the condition. This approach is combined with both bottom-up and top-down approaches to estimate expenditure for each cost component. The methodology is consistent with previously published research in this field in Australia and internationally.[13-15]

A targeted literature review was conducted to identify the prevalence of delirium in acute hospitalizations, nursing homes and in the community (without presenting to hospital). The targeted review was investigative in nature and considered fit-for-purpose as the prevalence and methods vary widely across studies. The focus of the literature review was on prevalence in a hospital setting. For hospitalizations, studies were included if they provided results for general medical or surgical wards (i.e. an acute setting) for the duration of the hospital stay using validated diagnostic measures. Results from the literature searches were pooled to estimate an average prevalence that could be applied to Australian hospital separations (Additional File 1).

No prevalence studies in Australian nursing homes were identified. Prevalence results were thus derived from a study from the Netherlands,[16] due to similarities in aged care settings, demographic profiles and medication prescribing rates – for example, both countries exhibit high rates of psychotropic medication prescribing (though there are some differences in the preferred antipsychotic agent),[17] despite their limited efficacy and adverse effects in people with delirium.[6] The combined prevalence and incidence was 8.5% and 16.9 per 100 person-years respectively. These rates are similar to the rates reported in other international literature.[18-20]

The total prevalence of delirium in Australia 2016-17 was adjusted to avoid double counting people in the residential aged care cohort who also present to hospital (Additional File 1).

Average duration of an episode of delirium and mortality

A targeted literature review was conducted to identify studies that reported the average duration of delirium across hospital and residential aged care settings. The average duration of delirium was estimated by taking a weighted average of the findings reported in twelve studies (Additional File 1). Mortality associated with delirium was estimated using an attributable fraction approach (Additional File 1) based on a previous systematic review and meta-analysis.[3]

Health care system expenditure

A targeted literature review was conducted to identify studies that reported cost inputs suitable to estimate health care system expenditure. The review was

considered more fit-for-purpose than a systematic review given this was a cost of illness study where many of the inputs are in data sets and grey literature (e.g. government documents), not in peer-reviewed literature.

Health system costs were estimated using a bottom-up approach. This includes costs associated with hospital, medication, and research expenditure, out of hospital medical and other health professionals' expenditure, and residential aged care expenditure. Delirium induces functional decline, resulting in a longer length of stay (LOS) for older people in hospital, consequently leading to higher hospitalization expenditure.[2] To estimate the additional expenditure, the prevalence of delirium among hospitalized older people was applied to the additional LOS and the average daily cost of care in a hospital setting. Cost data was sourced from the Australian Institute of Health and Welfare and the Independent Hospital Pricing Authority, who have responsibility for reporting on health expenditure in Australia (Additional File 1).

To estimate health research expenditure on delirium in Australia in 2016-17, this report utilized the National Health and Medical Research Council (NHMRC) grants database. The database outlines all NHMRC research grant funding between 2000 and 2016 and provides a description of the projects and key outcomes achieved.[21] Annual funding allocated to delirium research in 2016-17 was estimated by taking an average across the historical years. Other forms of health research where research costs can be recovered – for example, by charging a higher price for services – were not considered in this analysis, consistent with standard methodology.[12]

Out of hospital medical expenditure (GP consultations) was estimated by applying the average cost per GP consultation[22] to the total services associated with delirium.[23] Residential aged care expenditure was estimated using an attributable fraction approach based on literature to estimate admissions to aged care due to cognitive decline associated with delirium (Additional File 1). The number of admissions was adjusted by average LOS in residential aged care in Australia and applied to the average costs associated with residential aged care.

Other financial costs

The economic cost of short run productivity losses associated with absenteeism were estimated using the friction cost method (Additional File 1). The dollar value of informal care was estimated by using the opportunity cost method (Additional File 1). The additional cost of funerals borne by family and friends of people with delirium was based on the number of deaths associated with delirium (Additional File 1). The cost of a funeral was assumed to be £4,602. Funeral costs were brought forward by the average life expectancy at age of death. The deadweight losses due to lost taxation revenue (given an assumption of no change in spending) and additional government spending on delirium was calculated by applying the average marginal excess burden of taxation of £0.31 per £1 of tax.[24, 25]

Loss of wellbeing

Burden of disease methodology was employed to quantify the impact of delirium on wellbeing. The approach is non-financial, where pain, suffering and premature mortality are measured in terms of disability adjusted life years (DALYs). DALYs are

comprised of years of healthy life lost due to morbidity (YLDs) and years of life lost due to premature mortality (YLLs). YLDs were calculated using a prevalence approach, whereby the disability weight was multiplied by average duration of delirium. The disability weight for delirium used in this study was 0.17.[26] Duration of delirium was based on the prevalence of persistent delirium over 12 months.[27] DALYs were converted to a monetary value using the value of a statistical life year (£93,882), which is an official estimate updated for inflation.[28]

Costs of dementia attributable to delirium

Costs of dementia were sourced from an Australian cost of illness study.[29] Inputs were taken for Australia in the 2016 financial year, and updated using either health inflation or the Consumer Price Index as appropriate. The wellbeing cost attributable to dementia for YLLs or YLDs was estimated using data from the AIHW's Australian Burden of Disease Study.[30] The proportion of dementia attributable to delirium was estimated using the population attributable fraction approach (Additional File 1).

Sensitivity analysis

One-way sensitivity analyses were conducted on prevalence, the risk for mortality, dementia admission to aged care, average hospital costs, discount rate for DALYs, and the value of a statistical life year. The specific values represent the upper and lower 95% confidence intervals for the relevant input parameters where available, or unit costs that were 25% higher or lower if the distribution was unknown.

Currency standardization

All costs are expressed in 2016-17 pound sterling. Costs were converted from Australian dollars using the 2017 Organisation for Economic Cooperation and Development purchasing power parity of 2.065 Australian dollars per pound sterling in 2017.[31]

RESULTS

Health care system expenditure

There were estimated to be 132,595 occurrences of delirium in Australia in 2016-17. Delirium most commonly occurred in hospitals, with an estimated 119,760 cases. Total health system and aged care costs associated with delirium in Australia were estimated to be £844.2 million in 2016-17. The total comprised hospital (£247.3 million), residential aged care (£596.2 million), out-of-hospital medical (£0.4 million), and research expenditure (£0.3 million).

Other financial costs

Other financial costs – including absenteeism costs (£6.6 million), informal care costs (£0.8 million), brought forward funeral costs (£0.7 million) and deadweight losses (£188.4 million) – for people with delirium were estimated to be £196.6 million in Australia in 2016-17. Productivity losses imposed by delirium were estimated to be relatively small. The cost of informal care (£0.8 million) was relatively small due to the low opportunity cost of carer time (£0.84 per hour); informal carers provided 987,958 hours of care (see Additional file 1 for methods).

Loss of wellbeing

The total burden of disease from delirium in 2016-17 was estimated to be £994.1 million. Overall, people with delirium experienced: 5,441 years of healthy life lost due to disability (YLDs), or 0.041 YLDs per person with delirium; 5,687 years of life lost due to premature death (YLLs), or 0.043 YLLs per person with delirium; and 11,128 DALYs overall, or around 0.084 DALYs per person with delirium in 2016-17.

Costs of dementia attributable to delirium

Overall, it was estimated that 40,981 or 10.6% cases of dementia were attributable to delirium, which largely occur in people aged 85 years or older (Additional file 1). The total costs of dementia due to delirium were estimated to be £2.2 billion, of which the financial costs were £675.7 million and the loss of wellbeing was £1.6 billion. Table 1 shows cost breakdowns by age and gender group. Figure 1 shows the costs of dementia due to delirium broken down by health system and aged care costs, other financial costs and burden of disease.

Table 1. Costs of delirium in Australia in 2016-17, by age and gender group, £ million

Age/ gender	***Financial cost***		***Wellbeing cost***		***Total***
Male	**Delirium**	**Dementia due to delirium**	**Delirium**	**Dementia due to delirium**	
<65	15.0	-	19.5	-	**34.5**
65-69	8.1	7.9	12.6	5.1	**33.7**
70-74	57.5	22.3	26.8	18.2	**124.8**
75-89	81.9	48.2	43.7	67.6	**241.4**
80-84	124.6	67.9	89.5	126.3	**408.4**
85+	233.5	154.1	260.6	368.2	**1,016.3**
Female					
<65	14.7	-	18.7	-	**33.4**
65-69	7.0	9.8	10.8	7.2	**34.8**
70-74	52.2	14.6	22.4	13.8	**103.0**
75-79	81.0	47.1	39.7	72.2	**240.0**
80-84	121.9	71.1	80.3	144.0	**417.4**

85+	243.3	232.9	369.4	729.0	**1,574.6**
Overall	**1,040.8**	**675.7**	**994.1**	**1,551.6**	**4,262.2**

(INSERT FIGURE 1)

Total costs

The total costs of delirium in Australia were estimated to be £4.3 billion (AUD8.8 billion) in 2016-17. The total cost comprised financial costs of £1.7 billion (AUD3.5 billion) and the value of healthy life lost of £2.5 billion (AUD5.3 billion). Table 2 shows the costs of delirium broken down by health system and aged care costs, other financial costs, and burden of disease.

Table 2. Costs of delirium in Australia in 2016-17, by cost component

Cost component	***Total (£ million)***	***Per person with delirium (£)***
Health system and aged care	1,299.9	9,804
Other financial costs	416.6	3,142
Loss of wellbeing	2,545.7	19,199
Total costs	**4,262.2**	**32,145**

Sensitivity analysis

The results and specific values for the sensitivity analysis are shown in Table 3 and Figure 2. The total cost of delirium in Australia was most sensitive to changes in the risk for dementia following delirium and the overall prevalence rate. The total cost of delirium was estimated to range from £2.6 billion to £5.9 billion in Australia in 2016-17.

Table 3. Sensitivity analysis, £ million

Variable	*Financial*	*Loss of wellbeing*	*Total*
Base case	1,716.5	2,545.7	4,262.2
Prevalence (20.2%)			
Lower (17.0%)	1,333.3	2,110.6	3,443.9
Upper (23.3%)	2,141.1	2,993.6	5,134.7
Risk for mortality (OR = 1.77)			
Upper (OR = 2.15)	1,716.8	2,757.9	4,474.8
Lower (OR = 1.39)	1,716.2	2,316.7	4,032.9
Risk for dementia (OR for >65 = 5.88, OR for >85 = 7.56)			
Upper (OR for >65 = 20.70, OR for >85 = 29.43)	2,191.0	3,678.2	5,869.2
Lower (OR for >65 = 1.69, OR for >85 = 1.96)	1,213.0	1,372.8	2,585.8
Risk for admission to aged care (OR = 2.41)			
Upper (OR = 3.29)	1,993.3	2,545.7	4,539.0
Lower (OR = 1.77)	1,453.8	2,545.7	3,999.6
Average hospital costs*			
Upper (+25%)	1,794.7	2,545.7	4,340.4
Lower (-25%)	1,638.4	2,545.7	4,184.1
Discount rate for DALYs (3%)			
Upper (7%)	1,716.5	2,488.6	4,205.1
Lower (0%)	1,716.5	2,596.3	4,312.9

* hospital costs were varied for delirium only, not dementia.

(INSERT FIGURE 2)

DISCUSSION

This is the first study to estimate the economic impact of delirium in the Australian population using cost of illness methodology. While a number of studies have examined the financial costs of delirium, they are generally limited to specific services or population subgroups.[4] There have been no previous attempts to estimate the cost of delirium taking into account both the financial and wellbeing

costs for the entire population, as this study has done. It is critical that such economic estimations are undertaken as they inform decision making.

According to our findings, delirium poses a substantial burden on society. Considering delirium alone, the economic costs were mostly incurred by the health and aged care systems (£844.2 million), representing close to 1.5% of total expenditure on health and aged care in Australia. As many high-income western countries are dealing with issues of aging demographics and cognitive impairment, our findings may be generalizable to other health and aged care systems. For example, previous research has found that delirium is associated with multiple adverse outcomes including increased length and cost of hospitalization, functional and cognitive decline, institutionalization, and mortality.[2-4, 32] These results have significant implications for governments, who aim to identify conditions with high social and financial costs for focused attention through public education and other initiatives that effect improvements in health status. The results of this study highlight the need for concerted, worldwide efforts to mitigate the impacts of this clinically significant and costly medical condition.

There were 132,595 occurrences of delirium in Australia in 2016-17, but data from the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity Database for 2015-16 indicate that as many as 1 in 5 cases are missed. This is supported by previous research which suggests that delirium is undiagnosed in a large number of cases, ranging from approximately 25% of cases up to 87.5% in cases where dementia is also present.[11] This has significant implications for clinical

practice as the outcomes of delirium are serious.[1] Future research could focus on techniques to improve the detection rate.

Dementia represents a significant cost to the economy of all countries; the cost of dementia due to delirium is therefore an important cost component of delirium. It has been estimated that 47 million people are living with dementia globally, with costs of £583 billion; moreover, prevalence is expected to triple over the next three decades.[33] Overall, the costs of dementia attributable to delirium more than doubled the total costs of delirium in Australia in 2016-17. We found that approximately 10.6% of dementia cases, and thus costs, are associated with delirium. Therefore, delirium imposes a large cost burden on residential aged care, due to the high prevalence of dementia and the strong relationships between cognitive impairment and aged care. There may be considerable opportunities to prevent some of the worldwide burden of dementia and improve the fiscal sustainability of health systems in the face of aging populations.

Care for delirium following discharge from hospital relies heavily on informal carers, who provided almost 1 million hours of care to people with delirium. As workforce participation increases and the propensity to care declines,[34] there is a risk that the care needs of people with delirium will either go unmet, or require additional government funding for aged care to meet their needs.

There are some limitations to this study. First, the methods outlined the use of a non-systematic search strategy, noting that this was fit-for-purpose when a number of inputs were derived from official Australian Government statistics. The estimates

presented should be interpreted with this in mind. Second, limited studies were found with appropriate methods to robustly estimate the prevalence of delirium in Australian hospital settings, but also in community or residential aged care settings. In order to minimize the impact of this limitation and the risk of double counting across studies, our analysis focused on delirium which met the full diagnostic criteria. Similarly, data paucity in some areas, such as out-of-hospital medical costs and productivity losses (employment outcomes) means that total estimates may be conservative. Given the methodology, the costs of delirium presented in this paper should be treated as an estimate only. More research, including observational studies in Australian settings, is required to understand the true costs incurred by people with delirium. However, a study that can capture costs across the health system and aged care settings in Australia will be technically challenging and may not be feasible due to the fragmented nature of the systems and data collection – particularly beyond the point at which people interact with the system. Finally, cost of illness studies provide guidance on the size of the problem, but are only useful for informing cost effective options for change when compared to the cost of such interventions. More work is needed to identify cost effective options to reduce the burden of delirium in Australia.

CONCLUSION

In summary, delirium imposes a substantial burden on Australian society – both in terms of financial costs associated with health system expenditure and a greater need for residential aged care due to the functional and cognitive decline associated

with delirium and dementia. The financial costs of delirium were largely borne by Australian governments due to the health system and aged care expenditure.

Further research should seek to understand the causes, treatment and prognosis of delirium, especially with regard to potential pathways from an episode of delirium to subsequent mortality outcomes and reduced cognitive functioning. Improving mortality outcomes and reducing decline in cognitive functioning would help to reduce the substantial financial and wellbeing costs of delirium.

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Author contributions:

LP, JS and GC designed the study. JS and JH collected the data. All authors contributed to the analysis and interpretation of the data. All authors read, commented on and approved the draft manuscript and reviewed the manuscript for important intellectual content. The sponsor was not directly involved in the findings of the research.

Conflicts of interest

The authors declare that they have no competing interests.

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Patient and public involvement

Patient and public were not involved in this study.

Data sharing statement

No additional data are available.

FIGURE LEGENDS

Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million.

Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016 17.

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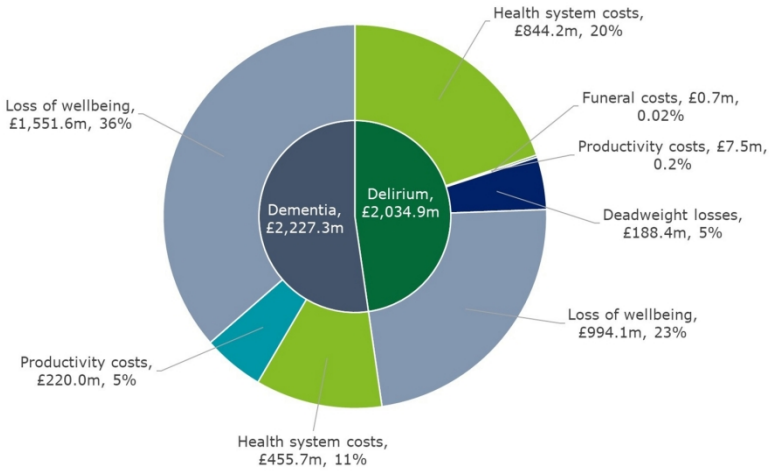

Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million

174x90mm (300 x 300 DPI)

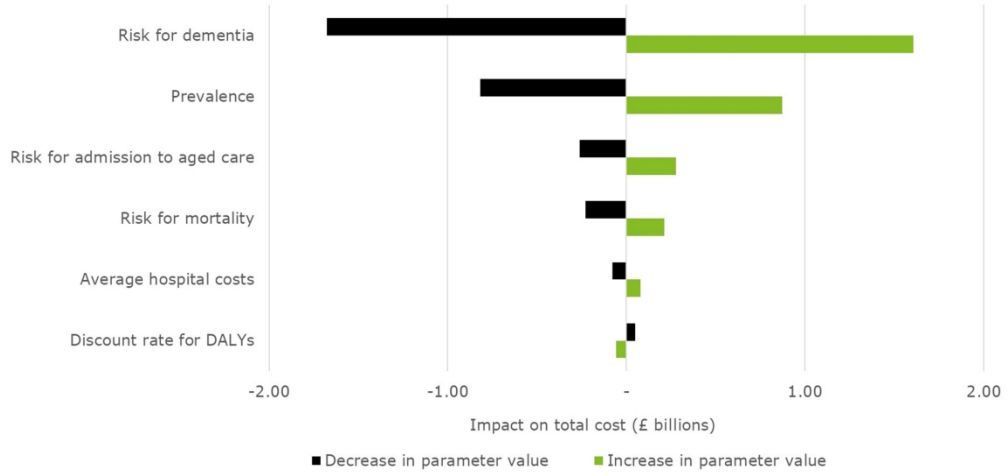

Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016-17

180x90mm (300 x 300 DPI)

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Additional File 1. Supplementary methods

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

1 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.

1.1 Prevalence in episodes of acute hospital care

There are numerous studies estimating the prevalence (generally at admission) and incidence (during hospitalisation) of delirium in hospitals. Prevalence on admission to hospital is typically for a cause other than delirium,[1] although delirium may still be present on admission to the emergency department.[2] Prevalence can vary widely depending on the type of hospital or the ward.[3] 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 1.1.

Table 1.1: 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

[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 (%)
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
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.

Patients in the included studies were admitted for more than one day. Based on data from the Australian Institute of Health and Welfare (AIHW),[17] it was estimated there 521,099 overnight acute emergency hospital separations for people aged 70 years or older in 2016-17. For elderly Australians, there were approximately 105,182[b] hospital separations involving delirium in 2016-17. There were an estimated 11,999 separations recorded as the principal diagnosis in 2016-17.[18]

Additional diagnosis separations in younger age groups (less than 70 years old) were estimated by applying the ratio between total and principal delirium diagnoses (105,182/11,999) to principal diagnoses in the younger age groups. Based on data from the AIHW,[17;18] there were estimated to be 1,663 separations where delirium was recorded as the principal diagnosis in separations for people

[b] 105,182 = 521,099 * 20.2%, noting small differences due to rounding.

aged less than 70 years old in 2016-17 (after adjusting for population growth). Thus, there were an estimated 14,578 separations for younger Australians, and 119,760 total cases of delirium in Australian hospitals in 2016-17.

1.2 Prevalence in residential aged care

Delirium is an important consideration in residential aged care, due to the high prevalence of dementia and the strong relationships between cognitive impairment and aged care. No studies of delirium in Australian residential aged care facilities were identified. As such, it was necessary to rely on international literature from countries with demographically similar profiles.

One of the largest and perhaps most comprehensive studies of delirium in aged care was conducted in the Netherlands,[19] although a number of studies have been undertaken in specific aged care facilities. The combined prevalence and incidence was 8.5% and 16.9 per 100 person-years respectively. These rates are similar to the rates reported in other international literature.[9;20;21]

In Australia on 30 June 2015, there were 172,044 permanent residents in aged care facilities. Using estimated population growth by age group from the Australian Bureau of Statistics (ABS),[22] it is expected that there will be 181,314 permanent residents in aged care facilities on 30 June 2017. Applying the prevalence (at baseline), and the incidence per 100 person years from Boorsma et al,[19,c] it was estimated that 46,054 permanent residents had delirium in 2016-17.

1.3 Adjusted prevalence estimates

There is potential for overlap in the prevalence estimates across hospital settings and residential aged care settings. As such, the prevalence estimates require adjustment to remove the double counting of people who had delirium in two care settings. A targeted literature search was conducted to estimate prevalence of delirium at admission and discharge from hospital, including information on dwelling characteristics (i.e. whether the person with delirium usually resides in

[c] It was assumed that each resident is in aged care for the full year, and so number of residents and person years are equal – i.e. no adjustments have been made for mortality in aged care facilities.

community or residential aged care). Based on the search, the following rates were used to adjust the prevalence to avoid double counting people in residential aged care who also present to hospital.

- 50% of cases were delirious at admission;[23]
- 43% of hospitalised patients were delirious at discharge;[7]
- 31.2% were admitted from residential aged care while 68.9% were admitted from the community;[15] and
- of people with delirium, 28% of patients were discharged to residential aged care, 63% were discharged to the community, and 9% died before discharge from hospital.[10]

Using the prevalence of delirium on admission to emergency departments (50% derived from Barron and Holmes[23]), it was estimated that 59,926 people were delirious in their usual setting before admission to hospital. Of these, 31.2% or 18,697 were admitted from residential aged care facilities.

Of the total hospital prevalence, it was estimated that 51,865 were still delirious at discharge based on McAvay et al,[7] and that 14,522 people were discharged to residential aged care with delirium (based on Inouye et al[10]). Thus, of the total prevalence in residential aged care (46,054), it was estimated that 33,219 people experienced delirium in hospital and residential aged care, while the remaining 12,835 did not present to hospital.

The total adjusted prevalence in Australia was therefore estimated to be 132,595, representing the total hospital prevalence and the episodes in aged care which were not hospitalised.

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Table 1.2: Total prevalence of delirium in Australia, 2016-17

Age / gender	Community	Residential aged care	Total
Male			
<65	3,278	1,756	5,034
65-69	1,916	1,281	3,197
70-74	4,342	2,088	6,430
75-89	6,282	2,868	9,149
80-84	9,680	3,545	13,225
85+	18,651	3,263	21,914
Total	*44,149*	*14,801*	*58,949*
Female			
<65	4,100	746	4,846
65-69	1,994	778	2,773
70-74	4,044	1,523	5,567
75-89	6,224	2,771	8,996
80-84	9,195	5,270	14,465
85+	16,835	20,164	36,999
Total	*42,393*	*31,253*	*73,646*
Total	**86,541**	**46,054**	**132,595**

Source: Authors calculations'. Note: components may not sum to totals due to rounding.

1.4 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 1.3).

Table 1.3: 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.

1.5 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 1.5).

Table 1.5: 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.[d]

[d] 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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2 Health and aged care system costs

2.1 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 estimate the additional expenditure, the prevalence of delirium among hospitalised patients was applied to the additional LOS and the average daily cost of care in a hospital setting.

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 as shown in 0. The change in LOS is similar to the average duration (5.9 days); however they may differ as people could develop an episode of delirium either before or following hospital and have days with delirium outside of a hospital setting.

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Table 2.1: 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 2.2: 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.

The average daily cost of an acute separation was obtained from the Independent Hospital Pricing Authority (IHPA) for 2014-15 and adjusted by the standard index rate used by IHPA (2.1%) to estimate the cost for the 2016-17 base year.[42] The average cost of any separation for 2016-17 was estimated to be $5,239, or $1,985 per day in 2016-17 terms.[e] The average daily cost was also adjusted by an additional 14.3% to inflate for non-allocated health costs (an allowance for capital costs) based on AIHW.[43] For:

[e] All costs are expressed in 2016-17 Australian dollars.

- a secondary diagnosis, the average daily cost was adjusted to remove separation costs that were unlikely to be attributable to delirium, such as costs associated with surgery[f]. The average daily cost for an additional separation was estimated to be $1,329, which was applied to hospital prevalence as an additional diagnosis (106,098) and the additional LOS (2.7 days); and
- a primary diagnosis (13,662 separations), the cost was assumed to be the same as the delirium diagnostic resource group, which was $9,268 in 2016-17 after updating for inflation in the National Efficient Price.[42]

2.2 Out of hospital medical and other health professional expenditure

There was limited evidence on the use of out of hospital medical and other health professional services in Australia. A study on psychosis related presentations to general practitioners (GPs) across Australia reported that 0.0175% of presentations were due to delirium,[g] although no evidence was found for presentations to a specialist or other health professionals.[44] Consequently, cost estimates are only presented for GPs.

The ratio of presentations to GPs was applied to Medicare Statistics data from the Department of Health's Summary Statistics by Broad Type of Service to estimate total GP consultations associated with delirium.[45] After adjusting for population growth, there were estimated to be 22,640 GP consultations associated with delirium in 2016-17.

The average cost of a GP service was calculated based on Medicare Statistics data.[45] The average cost was derived using the total benefits provided for non-referred attendances ($5.8 billion), the

[f] This included removing pathology, imaging, prosthesis, critical care, operating room, special procedure suite, emergency department, non clinical and depreciation costs. The costs included in adjusted daily cost were ward medical, ward nursing, allied health, on-costs, ward supplies, pharmacy and hotel. The adjustment removed approximately 47% the average daily cost of a separation.

[g] Referred to as "organic psychosis" in the paper.

number of services (129.37 million), the proportion of services which were bulk billed (83.7%), and the average out of pocket cost ($33.38)[h].

The average cost per consultation was estimated to be $51.13 in 2016-17 terms. However, patients may present to GPs with more than one problem, and therefore the entire cost is not directly attributable to delirium. The average cost ($51.13) was divided by the average number of problems (1.55) based on a report into General Practice Activity in Australia[i].[46] The cost per consultation attributable to delirium was therefore estimated to be $32.98 in 2016-17.

2.3 Residential aged care expenditure

Admission to residential aged care is a common outcome associated with delirium. A targeted literature review was conducted to estimate the likelihood of institutionalisation as a result of delirium. In a systematic review and meta-analysis of published studies that had controlled for confounding factors and illness severity, Witlox et al[31] reported that people with delirium have a 2.41 times greater chance of admission to aged care. The studies identified by Witlox et al[31] are summarised in Table 2.4.

[h] $(\text{Benefits} + (\text{Services} \times (1 - \frac{\text{Bulk billed rate}}{100}) \times \text{Out of pocket cost})$

[i] Britt et al[46] estimate an average number of problems of 1.55, total services were divided by this amount.

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Table 2.4: Risk of admission to aged care following delirium, outcomes at one year

Author, year (as cited in Witlox et al[31])	Country	Subgroup	Weighting (%)	Odds ratio (95% confidence interval)
Bellelli et al, 2008	Italy	Acute and rehabilitation wards	32.35	2.30 (1.33-3.98)
Bickel et al, 2008	Germany	General hospital; hip surgery patients	6.17	5.60 (1.60-19.65)
Giusti et al, 2006	Italy	Hospital, surgical	19.66	2.45 (1.21-4.95)
Pitkala et al, 2005	Finland	Hospital	5.61	0.93 (0.25-3.47)
McCusker et al, 2002	Canada	General medical	6.19	1.15 (0.33-4.05)
Inouye et al, 1998	Chicago, US	General medical	13.77	2.56 (1.10-5.93)
Inouye et al, 1998	Cleveland, US	General medical	2.74	8.60 (1.31-56.45)
Inouye et al, 1998	Yale, US	General medical	6.26	3.90 (1.12-13.56)
Francis and Kapoor, 1992	US	General medical	7.34	2.00 (0.63-6.33)
Pooled estimate				**2.41 (1.77-3.29)**

Source: Witlox et al[31] Note: the average follow up across the studies was 14.6 months.

Literature was found on the rates of institutionalisation for both those with delirium and those without. The results are summarised in Table 2.5. Across the studies included, the average rate of admission to aged care for people with delirium over one year of follow up was 46.8% compared with 23.3% for those without delirium.

Table 2.5: Rate of admission to aged care following hospitalisation, outcomes after one year

Author, year	Country	Sample characteristics	No delirium (N)	Delirium (N)	No delirium (%)	Delirium (%)
Adamis, 2006[24]	England	Elderly care unit;≥70 years	61	33	5.3	40.7
Cole, 1993[47]	Meta-analysis	Admissions to general medical ward; ≥60 years	665	60	8.3	43.2
Eeles, 2010[48]	UK	Admissions to general hospital; ≥75 years	175	103	17.6	40.5
Givens, 2009[49]	US	Admissions to general hospital, not delirious at admission; ≥70 years	72	18	26.1	46.2
McAvay, 2006[7]	US	Admissions to general hospital; >70 years	378	55	29.4	60.0
Total / weighted average			**1,351**	**269**	**16.2**	**45.5**

Source: as itemised in table.

The odds ratio was used to estimate the proportion of admissions to residential aged care which were due to delirium. To determine the cost, the number of admissions attributable to delirium was

multiplied by the average cost of residential aged care. The number of admissions attributable to delirium was derived using the methods outlined in Eide and Heuch.[50, j]

The average cost was estimated using the Aged Care Financing Authority (ACFA's) 2016 Report on the Funding and Financing of Aged Care.[51] The total expenditure on residential aged care services was $14.9 billion in 2014-15, or $90,793 per person in 2016-17 terms after dividing by the number of people in residential aged care and inflating to 2017 prices using the Consumer Price Index. The average cost per person was applied to the number of people admitted to residential aged care and adjusted by the total LOS, to arrive at the overall cost of residential aged care attributable to delirium

[j] First, the following two equations were solved simultaneously:

$$q1.s1 + q2.s2 = p1 \quad (1)$$

$$\frac{q1}{1-q1} * \frac{1-q_2}{q_2} = OR \quad (2)$$

where:

- q1 = probability of residential aged care placement given that an individual had delirium;
- q2 = probability of residential aged care placement given that an individual did not have delirium;
- s1 = probability of having delirium;
- s2 = probability of not having delirium;
- p1 = probability of residential aged care placement; and
- OR = odds ratio for admission to residential aged care given delirium.

After solving these equations for q1 and q2, the following equation gives the number of admissions to residential aged care which were attributable to delirium:

$PAF = \frac{(q1-q2).s1}{p1}$.

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3 Other financial costs

3.1 Absenteeism costs

People with delirium may be temporarily absent from paid employment due to being unwell during the episode of delirium. This may include days off to visit health professionals, during hospital admission, or days at home where they are not well enough to work.

The economic cost of short run productivity losses (temporary absenteeism) are estimated using the friction cost method, which estimates production losses for the time period required to restore production to levels before the case of delirium occurs. The friction cost method represents an employers' choice to make up lost production through overtime or employment of another employee that attracts a premium on the ordinary wage. The overtime premium represents lost employer profits, but also indicates how much an employer is willing to pay to maintain the same level of production. For this study it was assumed that the overtime rate is 40%.[52] The overtime premium is applied to average weekly earnings to estimate the total productivity losses.

Average employment rates and average weekly earnings for people with delirium are based on ABS data for the general population by age and gender.[53;54] This was used for all productivity loss calculations. From the literature, no studies could be located which estimated additional sick days for people with delirium. As such, the estimated duration of delirium (5.9 days) was used to inform time off work (assuming the person with delirium fully recovers before returning to work). Absenteeism estimates will only occur for people with delirium who usually reside in a community (as opposed to residential aged care) setting (prevalence of 86,541). Absenteeism costs were estimated by applying the duration to the prevalence occurring in the working age population, and adjusting for average employment rates and average weekly earnings.

3.2 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.

While informal carers are not paid for providing this care, informal care is not free in an economic sense. Time spent caring involves forfeiting time that could have been spent on paid work or undertaking leisure activities. As such, informal care can be valued as the opportunity cost associated with the loss of economic resources (labour) and the loss in leisure time valued by the carer. To estimate the dollar value of informal care, the opportunity cost method measures the formal sector productivity losses associated with caring, as time devoted to caring responsibilities is time which cannot be spent in the paid workforce.[k]

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.[l] As

[k] It is also possible to use the replacement cost method (which measures the cost of 'buying' an equivalent amount of care from the formal sector if the informal care was not supplied), and the self-valuation method (which measures how much carers themselves feel they should be paid for undertaking their responsibilities. However, these options were not explored further in this report.

[l] 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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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]

4 Dementia attributed to delirium

Epidemiological studies, and tissue, culture and animal studies, suggest that delirium leads to permanent cognitive decline and dementia.[59] A targeted literature review was conducted to identify studies analysing the causal link between dementia and delirium. Three studies were used to inform the odds of developing incident dementia following delirium:

- Lundstrom et al[60] estimated the odds ratio of developing new cases of dementia given delirium was 5.66.
- Davis et al[61] estimated the odds ratio of developing new cases of dementia given delirium was 8.65.
- Rockwood et al[62] estimated the odds ratio of developing new dementia given delirium was 5.97.

The sample for Davis et al was restricted to people over 85 years old, while Lundstrom et al and Rockwood et al included people over 65 years old. The weighted odds ratio (based on sample size) for people who are 65-84 years old was 5.88, while for people who are 85 years old or older, it was estimated to be 7.56. Using the population attributable fraction approach outlined in Eide and Heuch,[50] prevalence of delirium in our study and prevalence of dementia from Brown et al,[63] it was estimated that 40,981 (10.6%) of dementia cases were attributable to delirium.

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

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ABSTRACT

Objectives: To estimate the economic impact of delirium in the Australian population in 2016-17, including financial costs, and its burden on health.

Design, Setting and Participants: A cost of illness study was conducted for the Australian population in the 2016-17 financial year. The prevalence of delirium in 2016-17 was calculated to inform cost estimations. The costs estimated in this study also include dementia attributable to delirium.

Main outcome measures: The total and per capita costs were analyzed for three categories: health systems costs, other financial costs including productivity losses and informal care, and cost associated with loss of wellbeing (burden of disease). Costs were expressed in 2016-17 pound sterling (£) and Australian dollars (AUD).

Results: There were more than 132,000 occurrences of delirium in 2016-17, and more than 900 deaths were attributed to delirium in 2016-17. Delirium causes an estimated 10.6% of dementia in Australia. The total costs of delirium in Australia were estimated to be £4.3 billion (AUD8.8 billion) in 2016-17, ranging between £2.6 billion (AUD5.3 billion) and £5.9 billion (AUD12.1 billion). The total costs comprised financial costs of £1.7 billion and the value of healthy life lost of £2.5 billion. Dementia attributable to delirium accounted for £2.2 billion of the total cost of delirium.

Conclusions: These findings highlight the substantial burden that delirium imposes on Australian society - both in terms of financial costs associated with health system expenditure and the increased need for residential aged care due to the functional

and cognitive decline associated with delirium and dementia. To reduce the substantial wellbeing costs of delirium, further research should seek to better understand the potential pathways from an episode of delirium to subsequent mortality and reduced cognitive functioning outcomes.

Strengths and limitations of this study

- This cost of illness study estimates the total annual financial and wellbeing impacts of delirium for the first time in Australia.
- This study also estimates the costs of dementia that are associated with delirium in Australia, with significant implications for other high income western countries.
- This study is based on non-systematic search strategy to find relevant cost inputs, noting that a number of inputs are sourced from official Australian Government statistics.
- There were a number of data gaps when estimating costs, meaning the results of our study are only indicative of the total cost.
- Cost of illness studies provide guidance on the size of the problem, but more work is need to identify cost effective interventions to reduce the burden of delirium.

INTRODUCTION

Delirium is a common, serious, and sometimes fatal medical condition, characterized by an acute decline in cognitive functioning.[1] The term delirium is used to describe a transient, reversible neuropsychiatric syndrome that is of acute (abrupt or sudden) onset, with a fluctuating course which often occurs in the setting of a medical condition.[2] The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition characterizes delirium as a disturbance in attention, where the disturbance develops over a short period of time and represents an acute change from baseline attention and awareness. The disturbance should not be better explained by a pre-existing disorder, and evidence is required that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin.[3]

The development of delirium has been associated with increased morbidity, persistent functional decline, higher hospital costs, higher rates of residential aged care placement and increased mortality.[2, 4, 5] It is also a significant risk factor for later onset of dementia and acceleration of cognitive decline.[4] Though underdiagnosed, it is highly prevalent in hospitalizations, particularly so for palliative care populations[6, 7]; as many as 50% of people over the age of 65 who are admitted to hospital experience delirium depending on the clinical setting.[2] Despite being preventable in more than a third of cases, a study in Sweden showed that delirium remains a common complication in hospitalized elderly patients.[8]

A previous study in the United States, undertaken over a decade ago, assessed the costs associated with delirium after adjusting for patient sociodemographic and clinical characteristics and found that hospital costs per day for patients with delirium were more than double the costs of patients who did not experience an episode of delirium.[9] Additionally, previous studies have found associations between delirium and long-term cognitive impairment and dementia,[10] and premature death.[3, 11] However, the relative costs of these outcomes have not yet been established.

To date, no studies have estimated the costs of delirium in Australia. Understanding the costs of delirium is important because delirium is often missed in as many as two thirds of cases,[12] although there are validated tools for diagnosing delirium such as the Confusion Assessment Method.[2] By better understanding the costs, morbidity and mortality of delirium, it is possible to answer the question of whether it would be worthwhile to pay more attention to its prevention, diagnosis and treatment.

Different costs of disease are borne by different individuals or sectors of society. Understanding how the costs are shared helps to make informed decisions regarding interventions. The purpose of this study was to raise awareness of the impacts of delirium and contribute to improving policy in this area, by quantifying the magnitude of the economic burden associated with delirium in Australia in 2016-17.

METHODS

In this study, the financial costs of delirium to the Australian health system include the costs of running hospitals and nursing homes, GP and specialist services

reimbursed through Australia's universal health insurance scheme and private funds, the cost of pharmaceuticals and over-the-counter medications, allied health services, research and health administration. The other financial costs of delirium in this study include productivity costs, the cost of informal care, funeral costs, and deadweight losses associated with taxation payments and administration. The loss of wellbeing due to delirium was measured using disability adjusted life years (DALYs).

Prevalence

This cost of illness study was conducted using standard methodology,[13] based on a prevalence approach to cost measurement. Prevalence approaches measure the number of people with a given condition in a base period and the costs associated with treating them, as well as other financial and non-financial costs in that year due to the condition. This approach is combined with both bottom-up and top-down approaches to estimate expenditure for each cost component.[13] For example, a top-down approach has been used to estimate the costs of dementia due to delirium, while most costs of delirium have been established using a bottom-up approach. The methodology is consistent with previously published research in this field in Australia and internationally.[14-16] Costs were estimated from the perspective of Australian society for the 2016-17 financial year.

A targeted literature review was conducted to identify the prevalence of delirium in acute hospitalizations, nursing homes and in the community (without presenting to hospital). The targeted review was investigative in nature and considered fit-for-purpose as the prevalence and methods vary widely across studies. The focus of the

literature review was on prevalence in a hospital setting. For hospitalizations, studies were included if they provided results for general medical or surgical wards (i.e. an acute setting) for the duration of the hospital stay using validated diagnostic measures. Results from the literature searches were pooled by taking a weighted average to estimate an average prevalence that could be applied to Australian hospital separations (Additional File 1, Table 1). Overall, the prevalence of delirium in a hospital setting was estimated to be 20.2% on average, which was applied to the 521,099 overnight acute emergency hospital separations for people aged 70 years or older in 2016-17.[17] Therefore, there were approximately 105,182 hospital separations involving delirium in 2016-17, of which delirium was recorded as the principal diagnosis for approximately 11,999 separations in 2016-17.[18]

Additional diagnosis separations in younger age groups (less than 70 years old) were estimated by applying the ratio between total and principal delirium diagnoses to principal diagnoses in the younger age groups. [17,18] We estimate there were 14,578 separations for younger Australians, and 119,760 total cases of delirium in Australian hospitals in 2016-17.

No prevalence studies in Australian nursing homes were identified. Prevalence results were thus derived from a study from the Netherlands,[19] due to similarities in aged care settings, demographic profiles and medication prescribing rates – for example, both countries exhibit high rates of psychotropic medication prescribing (though there are some differences in the preferred antipsychotic agent),[20] despite their limited efficacy and adverse effects in people with delirium.[7] The combined prevalence and incidence was 8.5% and 16.9 per 100 person-years

respectively. These rates are similar to the rates reported in other international literature.[21-23]

In Australia on 30 June 2015, there were 172,044 permanent residents in aged care facilities. Using estimated population growth by age group from the Australian Bureau of Statistics (ABS),[24] we estimate there would have been 181,314 permanent residents in Australian aged care facilities on 30 June 2017. Applying the prevalence (at baseline), and the incidence per 100 person years from Boorsma et al,[19] we estimate that 46,054 permanent residents had delirium in 2016-17.

The total prevalence of delirium in Australia 2016-17 was adjusted to avoid double counting people in the residential aged care cohort who also present to hospital. The following rates were used to adjust the prevalence to avoid double counting people in residential aged care who also present to hospital: 50% of cases were delirious at admission;[25] 43% of hospitalized patients were delirious at discharge;[26] 31.2% were admitted from residential aged care while 68.9% were admitted from the community;[27] and of people with delirium, 28% of patients were discharged to residential aged care, 63% were discharged to the community, and 9% died before discharge from hospital.[28]

Average duration of an episode of delirium and mortality

A targeted literature review was conducted to identify studies that reported the average duration of delirium across hospital and residential aged care settings. The average duration of delirium was estimated by taking a weighted average of the

findings reported in twelve studies (Additional File 1, Table 2), which was 5.9 days on average.

Mortality associated with delirium was estimated using an attributable fraction approach,[13] and the hazard ratio of 1.77 used in our analysis was based on a previous systematic review and meta-analysis (Additional File 1, Table 3).[3]. The hazard ratio was used to estimate an attributable fraction for how many deaths are due to delirium in Australia.

Health care system expenditure

A targeted literature review was conducted to identify studies that reported cost inputs suitable to estimate health care system expenditure. The review was considered more fit-for-purpose than a systematic review given this was a cost of illness study where many of the inputs are in data sets and grey literature (e.g. government documents), not in peer-reviewed literature.

Health system costs were estimated using a bottom-up approach. This includes costs associated with hospital, medication, and research expenditure, out of hospital medical and other health professionals' expenditure, and residential aged care expenditure. Delirium induces functional decline, resulting in a longer length of stay (LOS) for older people in hospital, consequently leading to higher hospitalization expenditure.[2] To estimate the additional expenditure, the prevalence of delirium among hospitalized older people was applied to the additional LOS and the average daily cost of care in a hospital setting.

The average daily cost of an acute separation was obtained from the Independent Hospital Pricing Authority (IHPA) for 2014-15 and adjusted by the standard index rate used by IHPA (2.1%) to estimate the cost for the 2016-17 base year.[29] The average cost of any separation for 2016-17 was estimated to be £2,538, or £961 per day in 2016-17 terms. The average daily cost was also adjusted by an additional 14.3% to inflate for non-allocated health costs (an allowance for capital costs) based on AIHW.[30] Where delirium was a secondary diagnosis, the average daily cost was adjusted to remove separation costs that were unlikely to be attributable to delirium, such as costs associated with surgery. The average daily cost for an additional separation was estimated to be £644, which was applied to hospital prevalence as an additional diagnosis (106,098) and the additional LOS due to delirium, which was assumed to be 2.7 days (see Additional File 1, Table 4 and Additional File 1, Table 5). Where delirium was a primary diagnosis (13,662 separations), the cost was assumed to be the same as the delirium diagnostic resource group, which was £4,489 in 2016-17 after updating for inflation in the National Efficient Price.[29]

To estimate health research expenditure on delirium in Australia in 2016-17, this report utilized the National Health and Medical Research Council (NHMRC) grants database. The database outlines all NHMRC research grant funding between 2000 and 2016 and provides a description of the projects and key outcomes achieved.[31] Annual funding allocated to delirium research in 2016-17 was estimated by taking an average across the historical years. Other forms of health research where research

costs can be recovered – for example, by charging a higher price for services – were not considered in this analysis, consistent with standard methodology.[13]

Out of hospital medical expenditure (GP consultations) was estimated by applying the average cost per GP consultation (approximately £16 after adjusting for multiple problems per GP consultation),[32] to the total services associated with organic psychoses in Australia,[33] which was considered comparable to delirium. After adjusting for population growth, there were estimated to be 22,640 GP consultations associated with delirium in 2016-17.

Residential aged care expenditure was estimated using an attributable fraction approach based on literature to estimate admissions to aged care due to cognitive decline associated with delirium. The odds ratio for admission (2.41),[4] was converted to an attributable fraction. The number of admissions was adjusted by average LOS in residential aged care in Australia and applied to the average costs associated with residential aged care, which was estimated to be £43,978 per person based on the total expenditure on residential aged care services in Australia.[34]

Other financial costs

The economic cost of short run productivity losses associated with absenteeism were estimated using the friction cost method.[13] Average employment rates and average weekly earnings for people with delirium are based on ABS data for the general population by age and gender.[35, 36] Absenteeism was estimated as the duration of delirium (5.9 days) for separations that occur in the working age population, adjusted for employment rates.

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. On average, we estimate that each person with delirium would have received an additional 0.9 hours of care per week, based on the change in activities of daily living over a period of 12 months (Additional File 1 provides supplementary information that was used to estimate the additional hours of care).[37, 38] The dollar value of informal care was estimated as the opportunity cost of a carer's time, which was based on general population average weekly earnings and employment rates.[35, 36]

The additional cost of funerals borne by family and friends of people with delirium was based on the number of deaths associated with delirium. The cost of a funeral was assumed to be £4,602. Funeral costs were brought forward by the average life expectancy at age of death. The deadweight losses due to lost taxation revenue (given an assumption of no change in spending) and additional government spending on delirium was calculated by applying the average marginal excess burden of taxation of £0.31 per £1 of tax.[39, 40]

Loss of wellbeing

Burden of disease methodology was employed to quantify the impact of delirium on wellbeing.[41] The approach is non-financial, where pain, suffering and premature mortality are measured in terms of disability adjusted life years (DALYs). DALYs are comprised of years of healthy life lost due to morbidity (YLDs) and years of life lost due to premature mortality (YLLs).[41] YLDs were calculated using a prevalence

approach, whereby the disability weight was multiplied by average duration of delirium. The disability weight for delirium used in this study was 0.17.[42] Duration of delirium was based on the prevalence of persistent delirium over 12 months.[43] DALYs were converted to a monetary value using the value of a statistical life year (£93,882), which is an official estimate updated for inflation using the Consumer Price Index.[44] The value of a statistical life year was discounted at a rate of 3% per annum where it has been applied to future years of life lost due to morality from delirium.

Costs of dementia attributable to delirium

Costs of dementia were sourced from an Australian cost of illness study.[45] Inputs were taken for Australia in the 2016 financial year, and updated using either health inflation or the Consumer Price Index as appropriate. The wellbeing cost attributable to dementia for YLLs or YLDs was estimated using data from the Australian Institute of Health and Welfare's Australian Burden of Disease Study.[46] The proportion of dementia attributable to delirium was estimated using the population attributable fraction approach. The odds ratio for developing a new case was 5.88 for people aged 65-84 years old and 7.56 for people aged 85 years or older,[47-49] which was used to estimate an attributable fraction.

Sensitivity analysis

One-way sensitivity analyses were conducted on prevalence, the risk for mortality, dementia admission to aged care, average hospital costs, discount rate for DALYs, and the value of a statistical life year. The specific values represent the upper and

lower 95% confidence intervals for the relevant input parameters where available, or unit costs that were 25% higher or lower if the distribution was unknown.

Currency standardization

All costs are expressed in 2016-17 pound sterling. Costs were converted from Australian dollars using the 2017 Organisation for Economic Cooperation and Development purchasing power parity of 2.065 Australian dollars per pound sterling in 2017.[50]

Data analysis and ethical considerations

Data for this study was collected throughout January to June 2017 by the authors from a range of public data sources and literature. The data was analyzed and compiled in Microsoft Excel. No individual patient data was collected for the study and therefore, this study did not require ethics approval.

Patient and public involvement

Patient and public were not involved in this study.

RESULTS

Prevalence and mortality

There were an estimated 132,595 cases of delirium in Australia in 2016-17, representing both cases that occur in hospital and aged care. This is equivalent to approximately 0.5% of the population in Australia, although some individuals may experience delirium more than once in a year. Prevalence by age and gender are available in Table 1. The rates increase substantially with age.

Table 1. Prevalence of delirium in Australia, 2016-17

Age/ gender	*Community*	*Residential aged care*	*Total*	*% of general population*
Male				
<65	3,278	1,756	5,034	0.05
65-69	1,916	1,281	3,197	0.5
70-74	4,342	2,088	6,430	1.4
75-89	6,282	2,868	9,149	2.8
80-84	9,680	3,545	13,225	6.3
85+	18,651	3,263	21,914	11.8
Total	*44,149*	*14,801*	*58,949*	*0.5*
Female				
<65	4,100	746	4,846	0.05
65-69	1,994	778	2,773	0.5
70-74	4,044	1,523	5,567	1.1
75-79	6,224	2,771	8,996	2.5
80-84	9,195	5,270	14,465	5.5
85+	16,835	20,164	36,999	11.9
Total	*42,393*	*31,253*	*73,646*	*0.6*
Person	**86,541**	**46,054**	**132,595**	**0.5**

The hazard ratio for mortality indicated that 12,571 people who had delirium would die in 2016-17, and approximately 909 of these deaths were attributable to delirium itself.

Health care system expenditure

Delirium most commonly occurred in hospitals, with an estimated 119,760 cases (some of these individuals usually reside in aged care). Total health system and aged care costs associated with delirium in Australia were estimated to be £844.2 million in 2016-17. The total comprised hospital (£247.3 million), residential aged care (£596.2 million), out-of-hospital medical (£0.4 million), and research expenditure (£0.3 million).

Other financial costs

Other financial costs – including absenteeism costs (£6.6 million), informal care costs (£0.8 million), brought forward funeral costs (£0.7 million) and deadweight losses (£188.4 million) – for people with delirium were estimated to be £196.6 million in Australia in 2016-17. Productivity losses imposed by delirium were estimated to be relatively small. The cost of informal care (£0.8 million) was relatively small due to the low opportunity cost of carer time (£0.84 per hour); informal carers provided 987,958 hours of care.

Loss of wellbeing

The total burden of disease from delirium in 2016-17 was estimated to be £994.1 million. Overall, people with delirium experienced: 5,441 years of healthy life lost due to disability (YLDs), or 0.041 YLDs per person with delirium; 5,687 years of life lost due to premature death (YLLs), or 0.043 YLLs per person with delirium; and 11,128 DALYs overall, or around 0.084 DALYs per person with delirium in 2016-17.

Costs of dementia attributable to delirium

Overall, it was estimated that 40,981 or 10.6% cases of dementia were attributable to delirium, which largely occur in people aged 85 years or older. The total costs of dementia due to delirium were estimated to be £2.2 billion, of which the financial costs were £675.7 million and the loss of wellbeing was £1.6 billion. Table 2 shows cost breakdowns by age and gender group. Figure 1 shows the costs of dementia due to delirium broken down by health system and aged care costs, other financial costs and burden of disease.

Table 2. Costs of delirium in Australia in 2016-17, by age and gender group, £ million or %

Age/ gender	*Financial cost*		*Wellbeing cost*		*Total*	*% of total*
Male	**Delirium**	**Dementia due to delirium**	**Delirium**	**Dementia due to delirium**		
<65	15.0	-	19.5	-	34.5	1
65-69	8.1	7.9	12.6	5.1	33.7	1
70-74	57.5	22.3	26.8	18.2	124.8	3
75-89	81.9	48.2	43.7	67.6	241.4	6
80-84	124.6	67.9	89.5	126.3	408.4	10
85+	233.5	154.1	260.6	368.2	1,016.3	24
Female						
<65	14.7	-	18.7	-	33.4	1
65-69	7.0	9.8	10.8	7.2	34.8	1
70-74	52.2	14.6	22.4	13.8	103.0	2
75-79	81.0	47.1	39.7	72.2	240.0	6
80-84	121.9	71.1	80.3	144.0	417.4	10
85+	243.3	232.9	369.4	729.0	1,574.6	37
Overall	**1,040.8**	**675.7**	**994.1**	**1,551.6**	**4,262.2**	**100**
% of total	**24**	**16**	**23**	**36**	**100**	

(INSERT FIGURE 1)

Total costs

The total costs of delirium in Australia were estimated to be £4.3 billion (AUD8.8 billion) in 2016-17. The total cost comprised financial costs of £1.7 billion (AUD3.5 billion) and the value of healthy life lost of £2.5 billion (AUD5.3 billion). Table 3 shows the costs of delirium broken down by health system and aged care costs, other financial costs, and burden of disease.

Table 3. Costs of delirium in Australia in 2016-17, by cost component

Cost component	*Total (£ million)*	*Per person with delirium (£)*
Health system and aged care	1,299.9	9,804
Other financial costs	416.6	3,142
Loss of wellbeing	2,545.7	19,199
Total costs	**4,262.2**	**32,145**

Sensitivity analysis

The results and specific values for the sensitivity analysis are shown in Table 4 and Figure 2. The total cost of delirium in Australia was most sensitive to changes in the risk for dementia following delirium and the overall prevalence rate. The total cost of delirium was estimated to range from £2.6 billion to £5.9 billion in Australia in 2016-17.

Table 4. Sensitivity analysis, £ million

Variable	*Financial*	*Loss of wellbeing*	*Total*
Base case	1,716.5	2,545.7	4,262.2
Prevalence (20.2%)			
Lower (17.0%)	1,333.3	2,110.6	3,443.9
Upper (23.3%)	2,141.1	2,993.6	5,134.7
Risk for mortality (OR = 1.77)			
Upper (OR = 2.15)	1,716.8	2,757.9	4,474.8
Lower (OR = 1.39)	1,716.2	2,316.7	4,032.9
Risk for dementia (OR for >65 = 5.88, OR for >85 = 7.56)			
Upper (OR for >65 = 20.70, OR for >85 = 29.43)	2,191.0	3,678.2	5,869.2
Lower (OR for >65 = 1.69, OR for >85 = 1.96)	1,213.0	1,372.8	2,585.8
Risk for admission to aged care (OR = 2.41)			
Upper (OR = 3.29)	1,993.3	2,545.7	4,539.0
Lower (OR = 1.77)	1,453.8	2,545.7	3,999.6
Average hospital costs*			
Upper (+25%)	1,794.7	2,545.7	4,340.4
Lower (-25%)	1,638.4	2,545.7	4,184.1
Discount rate for DALYs (3%)			
Upper (7%)	1,716.5	2,488.6	4,205.1
Lower (0%)	1,716.5	2,596.3	4,312.9

* hospital costs were varied for delirium only, not dementia.

(INSERT FIGURE 2)

DISCUSSION

This is the first cost of illness study estimating the economic impact of delirium in the Australian population. While a number of studies have examined the financial costs of delirium, they are generally limited to specific services or population subgroups.[5] There have been no previous attempts to estimate the cost of delirium taking into account both the financial and wellbeing costs, as this study has done. It

is critical that such economic estimations are undertaken as they inform decision making.

According to our findings, delirium imposes a substantial burden on society. Considering delirium alone, the economic costs were mostly incurred by the health and aged care systems (£844.2 million), representing close to 1.5% of total expenditure on health and aged care in Australia. As many high-income western countries are dealing with issues of aging demographics and cognitive impairment, our findings may be generalizable to other health and aged care systems. For example, previous research has found that delirium is associated with multiple adverse outcomes including increased length and cost of hospitalization, functional and cognitive decline, institutionalization, and mortality.[2-5, 51] These results have significant implications for governments, who aim to identify conditions with high social and financial costs for focused attention through public education and other initiatives that effect improvements in health status. The results of this study highlight the need for concerted, worldwide efforts to mitigate the impacts of this clinically significant and costly medical condition.

According to our estimates, there were 132,595 occurrences of delirium in Australia in 2016-17, but data from the Australian Institute of Health and Welfare National Hospital Morbidity Database for 2015-16 indicate that as many as 1 in 5 cases are missed. This is supported by previous research which suggests that delirium is undiagnosed in a large number of cases, ranging from approximately 25% of cases up to 87.5% in cases where dementia is also present.[12] This has significant

implications for clinical practice as the outcomes of delirium are serious.[1] Future research could focus on techniques to improve the detection rate.

Dementia represents a significant cost to the economy of all countries; the cost of dementia due to delirium is therefore an important cost component of delirium. It has been estimated that 47 million people are living with dementia globally, with costs of £583 billion; moreover, prevalence is expected to triple over the next three decades.[52] Overall, the costs of dementia attributable to delirium more than doubled the total costs of delirium in Australia in 2016-17. We found that approximately 10.6% of dementia cases, and thus costs, are associated with delirium. Therefore, delirium imposes a large cost burden on residential aged care, due to the high prevalence of dementia and the strong relationships between cognitive impairment and aged care. There may be considerable opportunities to prevent some of the worldwide burden of dementia and improve the fiscal sustainability of health systems in the face of aging populations.

Care for delirium following discharge from hospital relies heavily on informal carers, who provided almost 1 million hours of care to people with delirium. As workforce participation increases and the propensity to care declines,[53] there is a risk that the care needs of people with delirium will either go unmet, or require additional government funding for aged care to meet their needs.

There are some limitations to this study. First, the methods outlined the use of a non-systematic search strategy, noting that this was fit-for-purpose when a number of inputs were derived from official Australian Government statistics. The estimates

presented should be interpreted with this in mind. Second, limited studies were found with appropriate methods to robustly estimate the prevalence of delirium in Australian hospital settings, but also in community or residential aged care settings. In order to minimize the impact of this limitation and the risk of double counting across studies, our analysis focused on delirium which met the full diagnostic criteria. Similarly, data paucity in some areas, such as out-of-hospital medical costs and productivity losses (employment outcomes) means that total estimates may be conservative. Given the methodology, the costs of delirium presented in this paper should be treated as an estimate only. More research, including observational studies in Australian settings, is required to understand the true costs incurred by people with delirium. However, a study that can capture costs across the health system and aged care settings in Australia will be technically challenging and may not be feasible due to the fragmented nature of the systems and data collection – particularly beyond the point at which people interact with the system. Finally, cost of illness studies provide guidance on the size of the problem, but are only useful for informing cost effective options for change when compared to the cost of such interventions. More work is needed to identify cost effective options to reduce the burden of delirium in Australia.

CONCLUSION

In summary, delirium imposes a substantial burden on Australian society – both in terms of financial costs associated with health system expenditure and a greater need for residential aged care due to the functional and cognitive decline associated

with delirium and dementia. The financial costs of delirium were largely borne by Australian governments due to the health system and aged care expenditure.

Further research should seek to understand the causes, treatment and prognosis of delirium, especially with regard to potential pathways from an episode of delirium to subsequent mortality outcomes and reduced cognitive functioning. Improving mortality outcomes and reducing decline in cognitive functioning would help to reduce the substantial financial and wellbeing costs of delirium.

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Author contributions:

LP, JS and GC conceived of and designed the study. JS, JH and LP collated the data, performed the data analysis and contributed to interpretation and reporting of the data. AT, MA and GC contributed to the interpretation and reporting of the data. All authors read, commented on and approved the final manuscript, and all authors reviewed the manuscript for important intellectual content. The sponsor was not directly involved in the findings of the research.

Conflicts of interest

The authors declare that they have no competing interests.

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Data sharing statement

No additional data are available.

FIGURE LEGENDS

Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million.

Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016 17.

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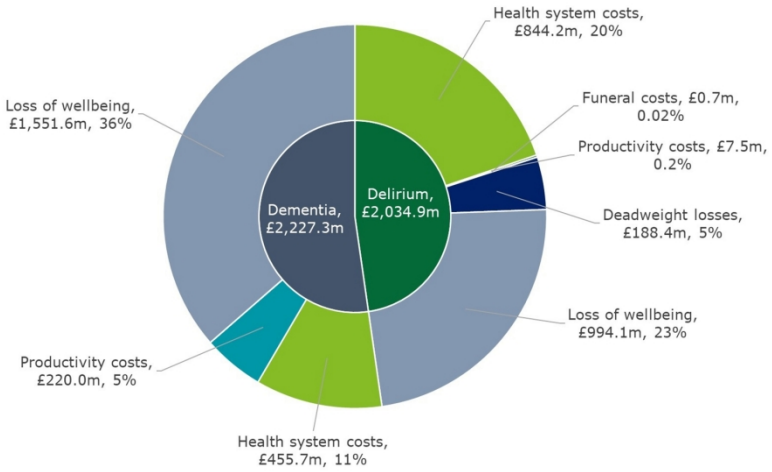

Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million

174x90mm (300 x 300 DPI)

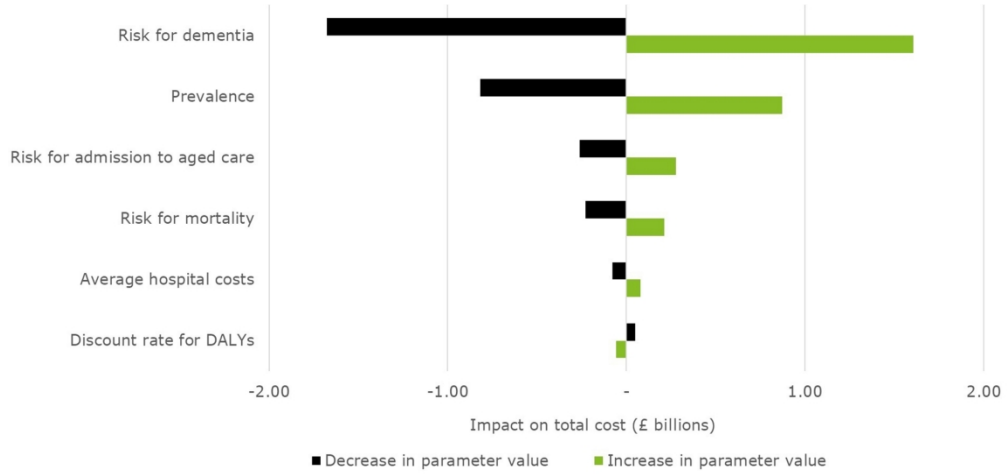

Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016-17

180x90mm (300 x 300 DPI)

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

Additional File 1. Supplementary methods

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

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 43-76.
		Present the study question and its relevance for health policy or practice decisions.	Page 5, line 77-81.
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 6, line 103-105.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 5, line 83-90.
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 6, line 101-102.
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 102.
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 12, line 243-245.
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 5, line 83-90.
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 158-245.
	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 172-208. Page 12, line 240-243. Page 13, line 263-266.
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 82-266.
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 82-266.
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 18, line 327-336.
	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 19, line 337-383.
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 23, line 426.
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 23, line 424.

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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[1]						
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[2]	US	>70 years	433	79.8 (6.3)	Daily	12.7
Holden, 2008[3]	New Zealand	>65 years	216	79.3	Every 2 days until discharge	29.1

[a] Three studies from Siddiqi et al[1] were removed from the analysis. Two of the studies were restricted to a sample of patients who were admitted from community dwellings),[4;5] 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.[2]

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Author, year	Country	Sample restrictions	Sample size	Mean age (SD)	Assessment frequency	Occurrence/ prevalence (%)
McCusker, 2003[6]	Canada	>65 years	1,552	83.6 (7.4)	-	22.3
Inouye, 1998[7]	US	>65 years, medical and surgical patients	107	-	Admission and discharge	25.0
Jones, 2006[8]	US	>70 years	491	79.0 (6.0)	Daily	22.0
Inouye, 1998[7]	US	>65 years, medical and surgical patients	174	-	Admission and discharge	15.0
Ryan 2013[9]	Ireland	Adults, no restriction	280		Point prevalence	17.6
Bellelli 2016[10]	Italy	>65 years	1,867	82 (7.4)	Point prevalence	22.9
Meagher 2014[11]	Ireland	Adults, no restriction	311	76 (13.1)	Point prevalence	16.7
Iseli 2007[12]	Australia	>65 years	104	80.1 (7.0)	At admission, follow up at 2-3 days, and then weekly	21.0
Travers 2013[13]	Australia	>70 years	493	80.4 (6.5)	Daily	17.3
Speed 2007[14]	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[1] 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[15]	England	Elderly care unit;≥70 years	94	82.8 (6.5)	8.6
Andrew, 2005[16]	Canada	Admissions to geriatric unit	77	78.5 (7.2)	6.3
O'Keeffe, 1997[17]	Ireland	Admissions to geriatric unit	94	83.2 (6.8)	7.0
Pandharipande, 2013[18]	US	Admissions to intensive care unit (ICU) with defined list of conditions; excluded those with recent ICU exposure	606	61	4.0
Rockwood, 1993[19]	Canada	Admissions to geriatric unit, mostly admitted from community	173	79 (8)	8.0
Van den Boogaard, 2012[20]	Netherlands	Admissions to ICU; excluded those admitted for < 1 day	272	81.7 (6.6)	2.0
Cole, 2012[21]	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.

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[22] 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[22])	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[22]

The hazard ratio (1.77) based on data from Witlox et al[22] 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

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.

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[23]	UK	Admissions to general hospital	590	6.0
Emond, 2017[24]	Canada	Admissions to ICU; ≥ 65 years	200	8.6
Gaudet, 1993[25]	France	Admissions to geriatric unit	487	18.0
Jitapunkul, 1992[26]	UK	Admissions to acute geriatric ward; ≥60 years	184	4.0
Kolbeinsson, 1993[27]	Iceland	Admissions to emergency ward; ≥70 years	272	2.9
McCusker, 2003[28]	Canada	Acute care; ≥65 years	359	3.6
O'Keeffe, 1997[17]	Ireland	Admissions to geriatric unit	225	10.0
Ramsay, 1991[29]	UK	Admissions to acute geriatric ward	119	-1.9
Rockwood, 1993[19]	Canada	Admissions to geriatric unit	173	4.0
Stevens, 1998[30]	Australia	Admissions to general medical	84	12
Tan, 2015[31]	New Zealand	>65 years	250	3.8
Thomas, 1988[32]	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[24]	Canada	Admissions to ICU; ≥ 65 years	200	8.6	8.4	0.98
Inouye, 1998[7]	US	≥65 years	727	1.2	0.5	0.42
McCusker, 2003[28]	Canada	Acute care; ≥65 years	359	4.5	0.5	0.10
O'Keeffe, 1997[17]	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.

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[33] 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.[34,35]

Analysis of the Survey of Disability, Ageing and Carers,[36] 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[37] and the chance of being employed.[38]

[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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BMJ Open

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ABSTRACT

Objectives: To estimate the economic impact of delirium in the Australian population in 2016-17, including financial costs, and its burden on health.

Design, Setting and Participants: A cost of illness study was conducted for the Australian population in the 2016-17 financial year. The prevalence of delirium in 2016-17 was calculated to inform cost estimations. The costs estimated in this study also include dementia attributable to delirium.

Main outcome measures: The total and per capita costs were analyzed for three categories: health systems costs, other financial costs including productivity losses and informal care, and cost associated with loss of wellbeing (burden of disease). Costs were expressed in 2016-17 pound sterling (£) and Australian dollars (AUD).

Results: There were an estimated 132,000 occurrences of delirium in 2016-17, and more than 900 deaths were attributed to delirium in 2016-17. Delirium causes an estimated 10.6% of dementia in Australia. The total costs of delirium in Australia were estimated to be £4.3 billion (AUD8.8 billion) in 2016-17, ranging between £2.6 billion (AUD5.3 billion) and £5.9 billion (AUD12.1 billion). The total estimated costs comprised financial costs of £1.7 billion and the value of healthy life lost of £2.5 billion. Dementia attributable to delirium accounted for £2.2 billion of the total cost of delirium.

Conclusions: These findings highlight the substantial burden that delirium imposes on Australian society - both in terms of financial costs associated with health system expenditure and the increased need for residential aged care due to the functional

and cognitive decline associated with delirium and dementia. To reduce the substantial wellbeing costs of delirium, further research should seek to better understand the potential pathways from an episode of delirium to subsequent mortality and reduced cognitive functioning outcomes.

Strengths and limitations of this study

- This cost of illness study estimates the total annual financial and wellbeing impacts of delirium for the first time in Australia.
- This study also estimates the costs of dementia that are associated with delirium in Australia, with significant implications for other high income western countries.
- This study is based on a non-systematic search strategy to find relevant cost inputs, noting that a number of inputs are sourced from official Australian Government statistics.
- There were a number of data gaps when estimating costs, meaning the results of this study are only indicative of the total cost.
- While this cost of illness study estimates the overall cost of delirium, more work is needed to identify cost effective interventions to reduce the burden of delirium.

INTRODUCTION

Delirium is a common, serious, and sometimes fatal medical condition, characterized by an acute decline in cognitive functioning.[1] The term delirium is used to describe a transient, reversible neuropsychiatric syndrome that is of acute (abrupt or sudden) onset, with a fluctuating course which often occurs in the setting of a medical condition.[2] The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition characterizes delirium as a disturbance in attention, where the disturbance develops over a short period of time and represents an acute change from baseline attention and awareness. The disturbance should not be better explained by a pre-existing disorder, and evidence is required that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin.[3]

The development of delirium has been associated with increased morbidity, persistent functional decline, higher hospital costs, higher rates of residential aged care placement and increased mortality.[2, 4, 5] It is also a significant risk factor for later onset of dementia and acceleration of cognitive decline.[4] Though underdiagnosed, it is highly prevalent in hospitalizations, particularly so for palliative care populations[6, 7]; as many as 50% of people over the age of 65 who are admitted to hospital experience delirium depending on the clinical setting.[2] Despite being preventable in more than a third of cases, a study in Sweden showed that delirium remains a common complication in hospitalized elderly patients.[8]

A previous study in the United States, undertaken over a decade ago, assessed the costs associated with delirium after adjusting for patient sociodemographic and clinical characteristics and found that hospital costs per day for patients with delirium were more than double the costs of patients who did not experience an episode of delirium.[9] Additionally, previous studies have found associations between delirium and long-term cognitive impairment and dementia,[10] and premature death.[3, 11] However, the relative costs of these outcomes have not yet been established.

To date, no studies have estimated the costs of delirium in Australia. Understanding the costs of delirium is important because delirium is often missed in as many as two thirds of cases,[12] although there are validated tools for diagnosing delirium such as the Confusion Assessment Method.[2]

By better understanding the costs, morbidity and mortality of delirium, it is possible to answer the question of whether it would be worthwhile to pay more attention to its prevention and diagnosis. Understanding the costs of delirium also helps to make informed decisions regarding treatment interventions. The purpose of this study was to raise awareness of the impacts of delirium and contribute to improving policy in this area, by quantifying the magnitude of the economic burden associated with delirium in Australia in 2016-17.

METHODS

This cost of illness study was conducted using standard methodology,[13] based on a prevalence approach to cost measurement. Prevalence approaches measure the

number of people with a given condition in a base period and the costs associated with treating them, as well as other financial and non-financial costs in that year due to the condition. This approach was combined with both bottom-up and top-down approaches to estimate expenditure for each cost component.[13] For example, a top-down approach was used to estimate the costs of dementia due to delirium, while most costs of delirium have been established using a bottom-up approach. The methodology is consistent with previously published research in this field in Australia and internationally.[14-16] Costs were estimated from the perspective of Australian society for the 2016-17 financial year.

In this study, the financial costs of delirium to the Australian health system include the costs of running hospitals and nursing homes, general practitioner (GP) and specialist services reimbursed through Australia's universal health insurance scheme and private funds, the cost of pharmaceuticals and over-the-counter medications, allied health services, research and health administration. The other financial costs of delirium in this study include productivity costs, informal care, funeral costs, and deadweight losses associated with taxation payments and administration. The loss of wellbeing due to delirium was measured using disability adjusted life years (DALYs).

A targeted literature review was conducted to identify the prevalence of delirium in acute hospitalizations, nursing homes and in the community (without presenting to hospital). The review also covered costs, productivity and other outcomes (e.g. mortality and burden of disease) due to delirium. The targeted review was investigative in nature and considered fit-for-purpose as the prevalence and

methods vary widely across studies. Searches were conducted using PubMed in June 2017.

Studies were included if they were conducted in a hospital setting, and covered general hospital wards (medical or surgical) reflective of an acute setting. Studies were also included if they included costs of delirium, including health system, productivity, carer and wellbeing costs. Studies were excluded from the analysis if they did not measure prevalence using validated diagnostic measures, or if they did not report on costs or outcomes from delirium. Studies were further excluded if they did not report on primary or administrative data. No specific date restrictions were applied to the literature review due to the investigative nature of it. The specific search terms used in the literature review are available in Additional File 1.

Results from the literature searches were generally pooled by taking a weighted average of outcomes or results. Additional grey literature (e.g. government statistics) were also collated and these documents provide many of the necessary inputs for this cost of illness study.

Prevalence

The prevalence of delirium in Australian hospitals was estimated by taking a weighted average across identified studies (see Additional File 1, Table 1). Prevalence was then applied to overnight acute emergency hospital separations for people aged 70 years or older in 2016-17 to estimate separations due to delirium in elderly people in that year.[17]

Additional diagnosis separations in younger age groups (less than 70 years old) were estimated by applying the ratio between total and principal delirium diagnoses to principal diagnoses in the younger age groups. [17,18]

No prevalence studies in Australian nursing homes were identified. Prevalence results were thus derived from a study from the Netherlands,[19] due to similarities in aged care settings, demographic profiles and medication prescribing rates – for example, both countries exhibit high rates of psychotropic medication prescribing (though there are some differences in the preferred antipsychotic agent),[20] despite their limited efficacy and adverse effects in people with delirium.[7] The combined prevalence and incidence was 8.5% and 16.9 per 100 person-years respectively. These rates are similar to the rates reported in other international literature.[21-23] These rates were applied to the number of permanent residents in aged care facilities in Australia, adjusting for population growth by age group from the Australian Bureau of Statistics (ABS).[24]

The total prevalence of delirium in Australia 2016-17 was adjusted to avoid double counting people in the residential aged care cohort who also present to hospital. The following rates were used to adjust the prevalence to avoid double counting people in residential aged care who also present to hospital: 50% of cases were delirious at admission;[25] 43% of hospitalized patients with delirium during their stay were delirious at discharge (5.5% delirious at discharge, 12.7% with delirium);[26] 31.2% were admitted from residential aged care while 68.9% were admitted from the community;[27] and of people with delirium, 28% of patients were discharged to

residential aged care, 63% were discharged to the community, and 9% died before discharge from hospital.[28]

Average duration of an episode of delirium and mortality

The average duration of delirium was estimated by taking a weighted average of the findings reported in twelve studies (Additional File 1, Table 2).

Mortality associated with delirium was estimated using an attributable fraction approach,[13] and a hazard ratio of 1.77 that was based on a previous systematic review and meta-analysis (Additional File 1, Table 3).[3]. The hazard ratio was used to estimate an attributable fraction for how many deaths are due to delirium in Australia.

Health care system expenditure

Health system costs were estimated using a bottom-up approach. This includes costs associated with hospital, medication, and research expenditure, out of hospital medical and other health professionals' expenditure, and residential aged care expenditure. Delirium induces functional decline, resulting in a longer length of stay (LOS) for older people in hospital, consequently leading to higher hospitalization expenditure.[2] To estimate the additional expenditure, the prevalence of delirium among hospitalized older people was applied to the additional LOS and the average daily cost of care in a hospital setting.

The average daily cost of an acute separation was obtained from the Independent Hospital Pricing Authority (IHPA) for 2014-15 and adjusted by the standard index rate used by IHPA (2.1%) to estimate the cost for the 2016-17 base year.[29] The

average daily cost was also adjusted by an additional 14.3% to inflate for non-allocated health costs (an allowance for capital costs) based on AIHW.[30]

Delirium can also be recorded as an additional diagnosis in Australian hospital data, where delirium contributes to a greater length of stay in hospital. The cost associated with an increased length of stay was estimated using the average daily cost of any hospital separation, which was further adjusted to remove separation costs that are unlikely to be attributable to delirium, such as costs associated with surgery. Where delirium was a primary diagnosis, the cost was assumed to be the same as the delirium diagnostic resource group, which was £4,489 in 2016-17 after updating for inflation in the National Efficient Price.[29]

Health research expenditure on delirium in Australia in 2016-17 was estimated using data from the National Health and Medical Research Council (NHMRC) grants database. The database outlines all NHMRC research grant funding between 2000 and 2016 and provides a description of the projects and key outcomes achieved.[31] Annual funding allocated to delirium research in 2016-17 was estimated by taking an average across the historical years. Other forms of health research where research costs can be recovered – for example, by charging a higher price for services – were not considered in this analysis, consistent with standard methodology.[13]

Out of hospital medical expenditure (GP consultations) was estimated by applying the average cost per GP consultation (approximately £16 after adjusting for multiple problems per GP consultation) to the total services associated with organic psychoses in Australia,[32, 33] which was considered comparable to delirium.

Residential aged care expenditure was estimated using an attributable fraction approach based on literature to estimate admissions to aged care due to cognitive decline associated with delirium. The odds ratio for admission (2.41),[4] was converted to an attributable fraction. The number of admissions was adjusted by average LOS in residential aged care in Australia and applied to the average costs associated with residential aged care, which is approximately £43,978 per person in aged care.[34]

Other financial costs

The economic cost of short run productivity losses associated with absenteeism were estimated using the friction cost method.[13] The absenteeism cost due to delirium was estimated by multiplying the average duration of delirium by the number of hospital separations that occur in the working age population, adjusted for general population employment rates. Average employment rates and average weekly earnings for people with delirium are based on ABS data for the general population by age and gender.[35, 36]

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. Evidence suggests that people with delirium experience a decline in functioning, such that they are unable to perform as many usual activities of daily living following delirium.[37, 38] Estimates of the hours of informal care provided to people with delirium was based on this expected decline in activities of daily living. The dollar value of informal care was estimated as the opportunity cost

of a carer's time, which was based on general population average weekly earnings and employment rates.[35, 36]

The additional cost of funerals borne by family and friends of people with delirium was based on the number of deaths associated with delirium. The cost of a funeral was assumed to be £4,602. Funeral costs were brought forward by the average life expectancy at age of death. The deadweight losses due to lost taxation revenue (given an assumption of no change in spending) and additional government spending on delirium was calculated by applying the average marginal excess burden of taxation of £0.31 per £1 of tax.[39, 40]

Loss of wellbeing

Burden of disease methodology was employed to quantify the impact of delirium on wellbeing.[41] The approach is non-financial, where pain, suffering and premature mortality are measured in terms of disability adjusted life years (DALYs). DALYs are comprised of years of healthy life lost due to morbidity (YLDs) and years of life lost due to premature mortality (YLLs).[41] YLDs were calculated using a prevalence approach, whereby the disability weight was multiplied by average duration of delirium. The disability weight for delirium used in this study was 0.17.[42] Duration of delirium was based on the prevalence of persistent delirium over 12 months.[43] DALYs were converted to a monetary value using the value of a statistical life year (£93,882), which is an official estimate updated for inflation using the Consumer Price Index.[44] The value of a statistical life year was discounted at a rate of 3% per

annum,[13] where it was applied to future years of life lost due to mortality from delirium.

Costs of dementia attributable to delirium

Costs of dementia were sourced from an Australian cost of illness study.[45] Inputs were taken for Australia in the 2016 financial year, and updated using either health inflation or the Consumer Price Index as appropriate. The wellbeing cost attributable to dementia for YLLs or YLDs was estimated using data from the Australian Institute of Health and Welfare's Australian Burden of Disease Study.[46] The proportion of dementia attributable to delirium was estimated using the population attributable fraction approach. The odds ratio for developing a new case was 5.88 for people aged 65-84 years old and 7.56 for people aged 85 years or older,[47-49] which was used to estimate the attributable fraction.

Sensitivity analysis

One-way sensitivity analyses were conducted on prevalence, the risk for mortality, dementia admission to aged care, average hospital costs, discount rate for DALYs, and the value of a statistical life year. The specific values represent the upper and lower 95% confidence intervals for the relevant input parameters where available, or unit costs that were 25% higher or lower if the distribution was unknown.

Currency standardization

All costs are expressed in 2016-17 pound sterling. Costs were converted from Australian dollars using the 2017 Organisation for Economic Cooperation and

Development purchasing power parity of 2.065 Australian dollars per pound sterling in 2017.[50]

Data analysis and ethical considerations

Data for this study was collected throughout January to June 2017 by the authors from a range of public data sources and literature. The data was analyzed and compiled in Microsoft Excel. No individual patient data was collected for the study and therefore, this study did not require ethics approval.

Patient and public involvement

Patient and public were not involved in the design or planning of this study.

RESULTS

Prevalence and mortality

Overall, the prevalence of delirium in a hospital setting was estimated to be 20.2% on average, which was applied to the 521,099 overnight acute emergency hospital separations for people aged 70 years or older in 2016-17. Therefore, there were an estimated 105,182 hospital separations involving delirium in 2016-17, of which delirium was recorded as the principal diagnosis for approximately 11,999 separations in 2016-17. In addition, there were an estimated 14,578 separations for younger Australians, and 119,760 total cases of delirium in Australian hospitals in 2016-17.

In Australia on 30 June 2015, there were 172,044 permanent residents in aged care facilities. There were an estimated 181,314 permanent residents in Australian aged

care facilities on 30 June 2017 after adjusting for population growth by age group. Applying the prevalence (at baseline), and the incidence per 100 person years from Boorsma et al,[19] it was estimated that 46,054 permanent residents had at least one episode of delirium in 2016-17.

After adjusting for the interactions between delirium in aged care and hospital settings, there were an estimated 132,595 cases of delirium in Australia in 2016-17, representing cases that occur in both settings. This is equivalent to approximately 0.5% of the population in Australia, although some individuals may experience delirium more than once in a year. Prevalence by age and gender are available in Table 1. The rates increase substantially with age.

Table 1. Estimated prevalence of delirium in Australia, 2016-17

Age/ gender	***Community***	***Residential aged care***	***Total***	***% of general population***
Male				
<65	3,278	1,756	5,034	0.05
65-69	1,916	1,281	3,197	0.5
70-74	4,342	2,088	6,430	1.4
75-89	6,282	2,868	9,149	2.8
80-84	9,680	3,545	13,225	6.3
85+	18,651	3,263	21,914	11.8
Total	*44,149*	*14,801*	*58,949*	*0.5*
Female				
<65	4,100	746	4,846	0.05
65-69	1,994	778	2,773	0.5
70-74	4,044	1,523	5,567	1.1
75-79	6,224	2,771	8,996	2.5
80-84	9,195	5,270	14,465	5.5
85+	16,835	20,164	36,999	11.9
Total	*42,393*	*31,253*	*73,646*	*0.6*
Person	**86,541**	**46,054**	**132,595**	**0.5**

The hazard ratio for mortality indicated that 12,571 people who had delirium would die, and an estimated 909 deaths were attributable to delirium itself in 2016-17.

Health care system expenditure

Delirium most commonly occurred in hospitals in Australia in 2016-17, with an estimated 119,760 cases (some of these individuals usually reside in aged care). Delirium was recorded as the primary diagnosis in 13,662 separations at an average cost of £4,489 per separation in 2016-17. Delirium was recorded as an additional diagnosis in a further 106,098 separations. The average daily cost for an additional separation was estimated to be £644, which was multiplied by the number of cases and the additional LOS due to delirium, which was estimated to be 2.7 days (see Additional File 1, Table 4 and Additional File 1, Table 5). After adjusting for population growth, there were estimated to be 22,640 GP consultations associated with delirium in 2016-17, which was multiplied by £16 per consultation to estimate total GP costs.

Total health system and aged care costs associated with delirium in Australia were estimated to be £844.2 million in 2016-17. The total comprised hospital (£247.3 million), residential aged care (£596.2 million), out-of-hospital medical (£0.4 million), and research expenditure (£0.3 million).

Other financial costs

On average, it was estimated that each person with delirium received an additional 0.9 hours of care per week, based on the change in activities of daily living over a period of 12 months (Additional File 1 provides supplementary information that was

used to estimate the additional hours of care). Thus, informal carers provided an estimated 987,958 hours of care in 2016-17, which was valued at £0.8 million. The cost of informal care (£0.8 million) is relatively small due to the low opportunity cost of carer time (£0.84 per hour).

We estimate that working age people with delirium were absent from work for 44,590 days in 2016-17, which was valued at £6.6 million using average weekly earnings for the general population.

Finally, brought forward funeral costs were estimated to be £0.7 million and deadweight losses were estimated to be £188.4 million in Australia 2016-17. Thus, total other financial costs (informal care, absenteeism, brought forward funeral costs and deadweight losses) were estimated to be £196.6 million in Australia in 2016-17. Productivity losses imposed by delirium were estimated to be relatively small as delirium largely occurs in the elderly population.

Loss of wellbeing

The total burden of disease from delirium in 2016-17 was estimated to be £994.1 million. Overall, delirium resulted in an estimated: 5,441 years of healthy life lost due to disability (YLDs), or 0.041 YLDs per person with delirium; 5,687 years of life lost due to premature death (YLLs), or 0.043 YLLs per person with delirium; and 11,128 DALYs overall, or around 0.084 DALYs per person with delirium in 2016-17.

Costs of dementia attributable to delirium

Overall, it was estimated that 40,981 or 10.6% cases of dementia were attributable to delirium, which largely occur in people aged 85 years or older. The total costs of

dementia due to delirium were estimated to be £2.2 billion in Australia in 2016-17, of which the financial costs were £675.7 million and the loss of wellbeing was £1.6 billion. Table 2 shows cost breakdowns by age and gender group. Figure 1 shows the costs of dementia due to delirium broken down by health system and aged care costs, other financial costs and burden of disease.

Table 2. Estimated costs of delirium in Australia in 2016-17, by age and gender group, £ million or %

Age/ gender	*Financial cost*		*Wellbeing cost*		*Total*	*% of total*
Male	**Delirium**	**Dementia due to delirium**	**Delirium**	**Dementia due to delirium**		
<65	15.0	-	19.5	-	34.5	1
65-69	8.1	7.9	12.6	5.1	33.7	1
70-74	57.5	22.3	26.8	18.2	124.8	3
75-89	81.9	48.2	43.7	67.6	241.4	6
80-84	124.6	67.9	89.5	126.3	408.4	10
85+	233.5	154.1	260.6	368.2	1,016.3	24
Female						
<65	14.7	-	18.7	-	33.4	1
65-69	7.0	9.8	10.8	7.2	34.8	1
70-74	52.2	14.6	22.4	13.8	103.0	2
75-79	81.0	47.1	39.7	72.2	240.0	6
80-84	121.9	71.1	80.3	144.0	417.4	10
85+	243.3	232.9	369.4	729.0	1,574.6	37
Overall	**1,040.8**	**675.7**	**994.1**	**1,551.6**	**4,262.2**	**100**
% of total	**24**	**16**	**23**	**36**	**100**	

(INSERT FIGURE 1)

Total costs

The total costs of delirium in Australia were estimated to be £4.3 billion (AUD8.8 billion) in 2016-17. The total cost comprised financial costs of £1.7 billion (AUD3.5 billion) and the value of healthy life lost of £2.5 billion (AUD5.3 billion).

Table 3 shows the costs of delirium broken down by health system and aged care costs, other financial costs, and burden of disease.

Table 3. Estimated costs of delirium in Australia in 2016-17, by cost component

Cost component	*Total (£ million)*	*Per person with delirium (£)*
Health system and aged care	1,299.9	9,804
Other financial costs	416.6	3,142
Loss of wellbeing	2,545.7	19,199
Total costs	**4,262.2**	**32,145**

Sensitivity analysis

The results and specific values for the sensitivity analysis are shown in Table 4 and Figure 2. The total cost of delirium in Australia was most sensitive to changes in the risk for dementia following delirium and the overall prevalence rate. The total cost of delirium was estimated to range from £2.6 billion to £5.9 billion in Australia in 2016-17.

Table 4. Sensitivity analysis, £ million

Variable	*Financial*	*Loss of wellbeing*	*Total*
Base case	1,716.5	2,545.7	4,262.2
Prevalence (20.2%)			
Lower (17.0%)	1,333.3	2,110.6	3,443.9
Upper (23.3%)	2,141.1	2,993.6	5,134.7
Risk for mortality (OR = 1.77)			
Upper (OR = 2.15)	1,716.8	2,757.9	4,474.8
Lower (OR = 1.39)	1,716.2	2,316.7	4,032.9
Risk for dementia (OR for >65 = 5.88, OR for >85 = 7.56)			
Upper (OR for >65 = 20.70, OR for >85 = 29.43)	2,191.0	3,678.2	5,869.2
Lower (OR for >65 = 1.69, OR for >85 = 1.96)	1,213.0	1,372.8	2,585.8
Risk for admission to aged care (OR = 2.41)			
Upper (OR = 3.29)	1,993.3	2,545.7	4,539.0
Lower (OR = 1.77)	1,453.8	2,545.7	3,999.6
Average hospital costs*			
Upper (+25%)	1,794.7	2,545.7	4,340.4
Lower (-25%)	1,638.4	2,545.7	4,184.1
Discount rate for DALYs (3%)			
Upper (7%)	1,716.5	2,488.6	4,205.1
Lower (0%)	1,716.5	2,596.3	4,312.9

* hospital costs were varied for delirium only, not dementia.

(INSERT FIGURE 2)

DISCUSSION

This is the first cost of illness study estimating the economic impact of delirium in the Australian population. While a number of studies have examined the financial costs of delirium, they are generally limited to specific services or population subgroups.[5] There have been no previous attempts to estimate the cost of delirium taking into account both the financial and wellbeing costs, as this study has done. It

is critical that such economic estimations are undertaken as they inform decision making.

According to these estimates, delirium imposes a substantial burden on society. Considering delirium alone, the economic costs were mostly incurred by the health and aged care systems (£844.2 million), representing close to 1.5% of total expenditure on health and aged care in Australia. As many high-income western countries are dealing with issues of aging demographics and cognitive impairment, the findings may be generalizable to other health and aged care systems. For example, previous research has found that delirium is associated with multiple adverse outcomes including increased length and cost of hospitalization, functional and cognitive decline, institutionalization, and mortality.[2-5, 51] These results have significant implications for governments, who aim to identify conditions with high social and financial costs for focused attention through public education and other initiatives that effect improvements in health status. The results of this study highlight the need for concerted, worldwide efforts to mitigate the impacts of this clinically significant and costly medical condition.

According to these estimates, there were 132,595 occurrences of delirium in Australia in 2016-17, but data from the Australian Institute of Health and Welfare National Hospital Morbidity Database for 2015-16 indicate that as many as 1 in 5 cases are missed. This is supported by previous research which suggests that delirium is undiagnosed in a large number of cases, ranging from approximately 25% of cases up to 87.5% in cases where dementia is also present.[12] This has significant

implications for clinical practice as the outcomes of delirium are serious.[1] Future research could focus on techniques to improve the detection rate.

Dementia represents a significant cost to the economy of all countries; the cost of dementia due to delirium is therefore an important cost component of delirium. It has been estimated that 47 million people are living with dementia globally, with costs of £583 billion in 2015 (original estimate converted from US dollars to pound sterling using purchasing power parity of 0.713);[50, 52] moreover, prevalence is expected to triple over the next three decades.[52] Overall, the costs of dementia attributable to delirium more than doubled the total costs of delirium in Australia in 2016-17. It was estimated that approximately 10.6% of dementia cases, and thus costs, are associated with delirium. Therefore, delirium imposes a large cost burden on residential aged care, due to the high prevalence of dementia and the strong relationships between cognitive impairment and aged care. There may be considerable opportunities to prevent some of the worldwide burden of dementia and improve the fiscal sustainability of health systems in the face of aging populations.

Care for delirium following discharge from hospital relies heavily on informal carers, who provided almost 1 million hours of care to people with delirium. As workforce participation increases and the propensity to care declines,[53] there is a risk that the care needs of people with delirium will either go unmet, or require additional government funding for aged care to meet their needs.

There are some limitations to this study. First, the methods outlined the use of a non-systematic search strategy, noting that this was fit-for-purpose when a number of inputs were derived from official Australian Government statistics. The estimates presented should be interpreted with this in mind. Second, limited studies were found with appropriate methods to robustly estimate the prevalence of delirium in Australian hospital settings, but also in community or residential aged care settings. In order to minimize the impact of this limitation and the risk of double counting across studies, the analysis focused on delirium which met the full diagnostic criteria. Similarly, data paucity in some areas, such as out-of-hospital medical costs and productivity losses (employment outcomes) means that total estimates may be conservative. Given the methodology, the costs of delirium presented in this paper should be treated as an estimate only. More research, including observational studies in Australian settings, is required to understand the true costs incurred by people with delirium. However, a study that can capture costs across the health system and aged care settings in Australia will be technically challenging and may not be feasible due to the fragmented nature of the systems and data collection – particularly beyond the point at which people interact with the system. Finally, cost of illness studies provide guidance on the size of the problem, but are only useful for informing cost effective options for change when compared to the cost of such interventions. More work is needed to identify cost effective options to reduce the burden of delirium in Australia.

CONCLUSION

In summary, delirium imposes a substantial burden on Australian society – both in terms of financial costs associated with health system expenditure and a greater need for residential aged care due to the functional and cognitive decline associated with delirium and dementia. The financial costs of delirium were largely borne by Australian governments due to the health system and aged care expenditure.

Further research should seek to understand the causes, treatment and prognosis of delirium, especially with regard to potential pathways from an episode of delirium to subsequent mortality outcomes and reduced cognitive functioning. Improving mortality outcomes and reducing decline in cognitive functioning would help to reduce the substantial financial and wellbeing costs of delirium.

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Author contributions:

LP, JS and GC conceived of and designed the study. JS, JH and LP collated the data, performed the data analysis and contributed to interpretation and reporting of the data. AT, MA and GC contributed to the interpretation and reporting of the data. All authors read, commented on and approved the final manuscript, and all authors reviewed the manuscript for important intellectual content. The sponsor was not directly involved in the findings of the research.

Conflicts of interest

The authors declare that they have no competing interests.

Funding sources

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Data sharing statement

No additional data are available.

FIGURE LEGENDS

Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million.

Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016 17.

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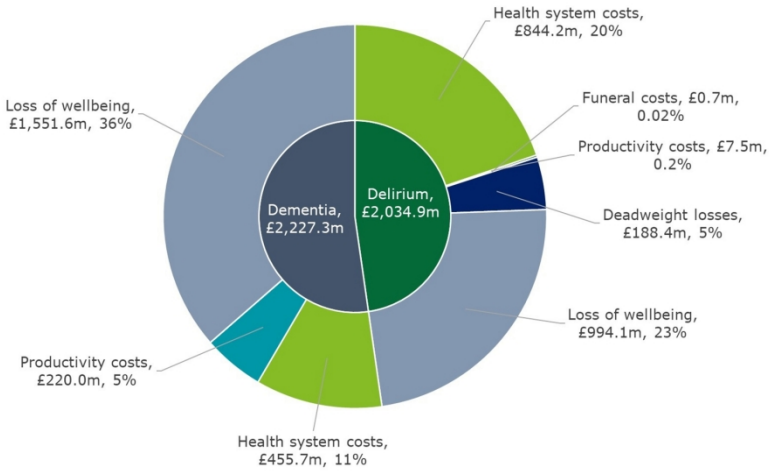

Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million

174x90mm (300 x 300 DPI)

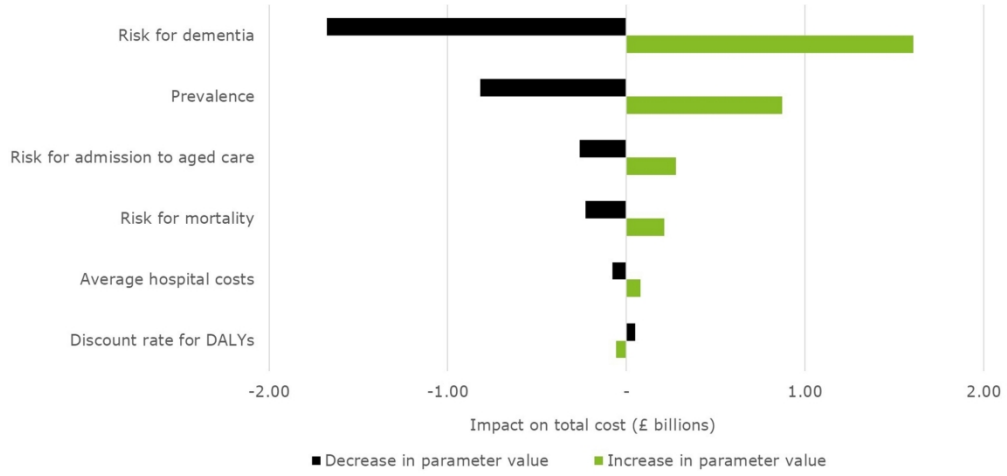

Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016-17

180x90mm (300 x 300 DPI)

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Additional File 1. Supplementary methods

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

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.

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

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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