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

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

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1 **ABSTRACT**

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

4 Design, Setting and Participants: A cost-of-illness study was conducted for the
5 Australian population in the 2016-17 financial year. The total cost of delirium was
6 estimated using standard cost-of-illness methodology. The prevalence of delirium in
7 2016-17 was calculated to inform cost estimations.

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

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

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

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3 23 understand the potential pathways from an episode of delirium to subsequent
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6 24 mortality and reduced cognitive functioning outcomes.
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12 26 **Strengths and limitations of this study**
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14

15 27 • This study uses cost of illness methodology to estimate the total annual financial
16
17 28 and wellbeing impacts of delirium for the first time in Australia.
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19
20 29 • This study also estimates the costs of dementia that are associated with delirium
21
22 30 in Australia, with significant implications for other high income western
23
24 31 countries.
25

26
27 32 • This study is based on non-systematic search strategy to find relevant cost
28
29 33 inputs, noting that a number of inputs are sourced from official Australian
30
31 34 Government statistics.
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34
35 35 • There were a number of data gaps when estimating costs, meaning the results of
36
37 36 our study are only indicative of the total cost.
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40 37 • Cost of illness studies provide guidance on the size of the problem, but more
41
42 38 work is need to identify cost effective interventions to reduce the burden of
43
44 39 delirium.
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40 INTRODUCTION

41 Delirium is a common, serious, and often-fatal medical condition, characterized by
42 an acute decline in cognitive functioning.[1] The term delirium is used to describe a
43 transient, reversible neuropsychiatric syndrome that is of acute (abrupt or sudden)
44 onset, with a fluctuating course which occurs in the setting of a medical condition.

45 Acute confusion or impaired cognition are other terms that are commonly used to
46 refer to delirium.[2]

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

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

1
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3 62 premature death.[3, 10] However, the relative costs of these outcomes have not yet
4
5
6 63 been established.
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8
9 64 To date, no studies have estimated the costs of delirium in Australia. Understanding
10
11 65 the costs of delirium is important because it is difficult to diagnose. There are no
12
13 66 diagnostic blood tests, x-rays or scans and hence it is often missed in as many as two
14
15
16 67 thirds of cases.[11] By better understanding the costs of delirium, it is possible to
17
18 68 answer the question of whether it would be worthwhile to pay more attention to its
19
20
21 69 prevention, diagnosis and treatment.
22

23
24 70 Financial costs of delirium to the Australian health system include the costs of
25
26 71 running hospitals and nursing homes, GP and specialist services reimbursed through
27
28
29 72 Australia's universal health insurance scheme and private funds, the cost of
30
31 73 pharmaceuticals and over-the-counter medications, allied health services, research
32
33
34 74 and health administration. Other financial costs of delirium include productivity
35
36 75 costs, the cost of informal care, funeral costs, and deadweight loss of taxation
37
38
39 76 payments and administration. The burden of disease associated with delirium
40
41 77 measures pain, suffering, and premature mortality in terms of disability adjusted life
42
43 78 years (DALYs). Different costs of disease are borne by different individuals or sectors
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45
46 79 of society. Understanding how the costs are shared helps to make informed
47
48
49 80 decisions regarding interventions.
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51
52 81 The purpose of this study was to raise awareness of the impacts of delirium and
53
54 82 contribute to improving policy in this area, by quantifying the magnitude of the
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3 83 economic burden associated with delirium in Australia in 2016-17 on the basis of
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6 84 cost-of-illness methodology.
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8 85 **METHODS**

9 86 **Prevalence**

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12 87 This study was conducted using standard cost-of-illness methodology,[12] based on
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14
15 88 a prevalence approach to cost measurement. Prevalence approaches measure the
16
17
18 89 number of people with a given condition in a base period and the costs associated
19
20
21 90 with treating them, as well as other financial and non-financial costs in that year due
22
23
24 91 to the condition. This approach is combined with both bottom-up and top-down
25
26
27 92 approaches to estimate expenditure for each cost component. The methodology is
28
29
30 93 consistent with previously published research in this field in Australia and
31
32
33 94 internationally.[13-15]

34
35
36 95 A targeted literature review was conducted to identify the prevalence of delirium in
37
38
39 96 acute hospitalizations, nursing homes and in the community (without presenting to
40
41
42 97 hospital). The targeted review was investigative in nature and considered fit-for-
43
44
45 98 purpose as the prevalence and methods vary widely across studies. The focus of the
46
47
48 99 literature review was on prevalence in a hospital setting. For hospitalizations, studies
49
50
51 100 were included if they provided results for general medical or surgical wards (i.e. an
52
53
54 101 acute setting) for the duration of the hospital stay using validated diagnostic
55
56
57 102 measures. Results from the literature searches were pooled to estimate an average
58
59
60 103 prevalence that could be applied to Australian hospital separations (Additional File
104 1).

1
2
3 105 No prevalence studies in Australian nursing homes were identified. Prevalence
4
5 106 results were thus derived from a study from the Netherlands,[16] due to similarities
6
7
8 107 in aged care settings, demographic profiles and medication prescribing rates – for
9
10 108 example, both countries exhibit high rates of psychotropic medication prescribing
11
12
13 109 (though there are some differences in the preferred antipsychotic agent),[17]
14
15 110 despite their limited efficacy and adverse effects in people with delirium.[6] The
16
17
18 111 combined prevalence and incidence was 8.5% and 16.9 per 100 person-years
19
20 112 respectively. These rates are similar to the rates reported in other international
21
22
23 113 literature.[18-20]

24
25
26 114 The total prevalence of delirium in Australia 2016-17 was adjusted to avoid double
27
28 115 counting people in the residential aged care cohort who also present to hospital
29
30
31 116 (Additional File 1).

32 33 117 **Average duration of an episode of delirium and mortality**

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35
36
37 118 A targeted literature review was conducted to identify studies that reported the
38
39 119 average duration of delirium across hospital and residential aged care settings. The
40
41
42 120 average duration of delirium was estimated by taking a weighted average of the
43
44 121 findings reported in twelve studies (Additional File 1). Mortality associated with
45
46 122 delirium was estimated using an attributable fraction approach (Additional File 1)
47
48
49 123 based on a previous systematic review and meta-analysis.[3]

50 51 52 124 **Health care system expenditure**

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54
55 125 A targeted literature review was conducted to identify studies that reported cost
56
57
58 126 inputs suitable to estimate health care system expenditure. The review was

1
2
3 127 considered more fit-for-purpose than a systematic review given this was a cost of
4
5
6 128 illness study where many of the inputs are in data sets and grey literature (e.g.
7
8 129 government documents), not in peer-reviewed literature.
9

10
11 130 Health system costs were estimated using a bottom-up approach. This includes costs
12
13
14 131 associated with hospital, medication, and research expenditure, out of hospital
15
16 132 medical and other health professionals' expenditure, and residential aged care
17
18 133 expenditure. Delirium induces functional decline, resulting in a longer length of stay
19
20
21 134 (LOS) for older people in hospital, consequently leading to higher hospitalization
22
23 135 expenditure.[2] To estimate the additional expenditure, the prevalence of delirium
24
25
26 136 among hospitalized older people was applied to the additional LOS and the average
27
28 137 daily cost of care in a hospital setting. Cost data was sourced from the Australian
29
30
31 138 Institute of Health and Welfare and the Independent Hospital Pricing Authority, who
32
33 139 have responsibility for reporting on health expenditure in Australia (Additional File
34
35
36 140 1).

37
38
39 141 To estimate health research expenditure on delirium in Australia in 2016-17, this
40
41 142 report utilized the National Health and Medical Research Council (NHMRC) grants
42
43 143 database. The database outlines all NHMRC research grant funding between 2000
44
45
46 144 and 2016 and provides a description of the projects and key outcomes achieved.[21]
47
48 145 Annual funding allocated to delirium research in 2016-17 was estimated by taking an
49
50
51 146 average across the historical years. Other forms of health research where research
52
53 147 costs can be recovered – for example, by charging a higher price for services – were
54
55
56 148 not considered in this analysis, consistent with standard methodology.[12]
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3 149 Out of hospital medical expenditure (GP consultations) was estimated by applying
4
5
6 150 the average cost per GP consultation[22] to the total services associated with
7
8 151 delirium.[23] Residential aged care expenditure was estimated using an attributable
9
10
11 152 fraction approach based on literature to estimate admissions to aged care due to
12
13 153 cognitive decline associated with delirium (Additional File 1). The number of
14
15 154 admissions was adjusted by average LOS in residential aged care in Australia and
16
17
18 155 applied to the average costs associated with residential aged care.

21 156 **Other financial costs**

23
24 157 The economic cost of short run productivity losses associated with absenteeism
25
26 158 were estimated using the friction cost method (Additional File 1). The dollar value of
27
28
29 159 informal care was estimated by using the opportunity cost method (Additional File
30
31 160 1). The additional cost of funerals borne by family and friends of people with
32
33
34 161 delirium was based on the number of deaths associated with delirium (Additional
35
36 162 File 1). The cost of a funeral was assumed to be £4,602. Funeral costs were brought
37
38
39 163 forward by the average life expectancy at age of death. The deadweight losses due
40
41 164 to lost taxation revenue (given an assumption of no change in spending) and
42
43
44 165 additional government spending on delirium was calculated by applying the average
45
46 166 marginal excess burden of taxation of £0.31 per £1 of tax.[24, 25]

49 167 **Loss of wellbeing**

51
52 168 Burden of disease methodology was employed to quantify the impact of delirium on
53
54 169 wellbeing. The approach is non-financial, where pain, suffering and premature
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56
57 170 mortality are measured in terms of disability adjusted life years (DALYs). DALYs are

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2
3 171 comprised of years of healthy life lost due to morbidity (YLDs) and years of life lost
4
5
6 172 due to premature mortality (YLLs). YLDs were calculated using a prevalence
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8 173 approach, whereby the disability weight was multiplied by average duration of
9
10 174 delirium. The disability weight for delirium used in this study was 0.17.[26] Duration
11
12
13 175 of delirium was based on the prevalence of persistent delirium over 12 months.[27]
14
15 176 DALYs were converted to a monetary value using the value of a statistical life year
16
17
18 177 (£93,882), which is an official estimate updated for inflation.[28]
19
20

21 178 **Costs of dementia attributable to delirium**

22
23
24 179 Costs of dementia were sourced from an Australian cost of illness study.[29] Inputs
25
26 180 were taken for Australia in the 2016 financial year, and updated using either health
27
28 181 inflation or the Consumer Price Index as appropriate. The wellbeing cost attributable
29
30 182 to dementia for YLLs or YLDs was estimated using data from the AIHW's Australian
31
32 183 Burden of Disease Study.[30] The proportion of dementia attributable to delirium
33
34 184 was estimated using the population attributable fraction approach (Additional File
35
36 185 1).
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41 186 **Sensitivity analysis**

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44
45 187 One-way sensitivity analyses were conducted on prevalence, the risk for mortality,
46
47 188 dementia admission to aged care, average hospital costs, discount rate for DALYs,
48
49 189 and the value of a statistical life year. The specific values represent the upper and
50
51 190 lower 95% confidence intervals for the relevant input parameters where available, or
52
53 191 unit costs that were 25% higher or lower if the distribution was unknown.
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58 192 **Currency standardization**

1
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3 193 All costs are expressed in 2016-17 pound sterling. Costs were converted from
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5 194 Australian dollars using the 2017 Organisation for Economic Cooperation and
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7
8 195 Development purchasing power parity of 2.065 Australian dollars per pound sterling
9
10
11 196 in 2017.[31]
12

13 14 197 **RESULTS**

15 16 17 198 **Health care system expenditure**

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19
20 199 There were estimated to be 132,595 occurrences of delirium in Australia in 2016-17.
21
22 200 Delirium most commonly occurred in hospitals, with an estimated 119,760 cases.
23
24 201 Total health system and aged care costs associated with delirium in Australia were
25
26 202 estimated to be £844.2 million in 2016-17. The total comprised hospital
27
28 203 (£247.3 million), residential aged care (£596.2 million), out-of-hospital medical (£0.4
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30 204 million), and research expenditure (£0.3 million).
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35 205 **Other financial costs**

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37
38 206 Other financial costs – including absenteeism costs (£6.6 million), informal care costs
39
40 207 (£0.8 million), brought forward funeral costs (£0.7 million) and deadweight losses
41
42 208 (£188.4 million) – for people with delirium were estimated to be £196.6 million in
43
44 209 Australia in 2016-17. Productivity losses imposed by delirium were estimated to be
45
46 210 relatively small. The cost of informal care (£0.8 million) was relatively small due to
47
48 211 the low opportunity cost of carer time (£0.84 per hour); informal carers provided
49
50 212 987,958 hours of care (see Additional file 1 for methods).
51
52
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55

56 213 **Loss of wellbeing**

214 The total burden of disease from delirium in 2016-17 was estimated to be
 215 £994.1 million. Overall, people with delirium experienced: 5,441 years of healthy life
 216 lost due to disability (YLDs), or 0.041 YLDs per person with delirium; 5,687 years of
 217 life lost due to premature death (YLLs), or 0.043 YLLs per person with delirium; and
 218 11,128 DALYs overall, or around 0.084 DALYs per person with delirium in 2016-17.

219 **Costs of dementia attributable to delirium**

220 Overall, it was estimated that 40,981 or 10.6% cases of dementia were attributable
 221 to delirium, which largely occur in people aged 85 years or older (Additional file 1).
 222 The total costs of dementia due to delirium were estimated to be £2.2 billion, of
 223 which the financial costs were £675.7 million and the loss of wellbeing was
 224 £1.6 billion. Table 1 shows cost breakdowns by age and gender group. Figure 1
 225 shows the costs of dementia due to delirium broken down by health system and
 226 aged care costs, other financial costs and burden of disease.

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

<i>Age/ gender</i>	<i>Financial cost</i>		<i>Wellbeing cost</i>		<i>Total</i>
	<i>Delirium</i>	<i>Dementia due to delirium</i>	<i>Delirium</i>	<i>Dementia due to delirium</i>	
Male					
<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

228

229 (INSERT FIGURE 1)

230 **Total costs**

231 The total costs of delirium in Australia were estimated to be £4.3 billion

232 (AUD8.8 billion) in 2016-17. The total cost comprised financial costs of £1.7 billion

233 (AUD3.5 billion) and the value of healthy life lost of £2.5 billion (AUD5.3 billion).

234 Table 2 shows the costs of delirium broken down by health system and aged care

235 costs, other financial costs, and burden of disease.

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

<i>Cost component</i>	<i>Total (£ million)</i>	<i>Per person with delirium (£)</i>
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

237

238 **Sensitivity analysis**

239 The results and specific values for the sensitivity analysis are shown in Table 3 and

240 Figure 2. The total cost of delirium in Australia was most sensitive to changes in the

241 risk for dementia following delirium and the overall prevalence rate. The total cost of

242 delirium was estimated to range from £2.6 billion to £5.9 billion in Australia in

243 2016-17.

244 Table 3. Sensitivity analysis, £ million

<i>Variable</i>	<i>Financial</i>	<i>Loss of wellbeing</i>	<i>Total</i>
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

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

246

247 (INSERT FIGURE 2)

248 DISCUSSION

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

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3 254 costs for the entire population, as this study has done. It is critical that such
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6 255 economic estimations are undertaken as they inform decision making.
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9 256 According to our findings, delirium poses a substantial burden on society.
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11 257 Considering delirium alone, the economic costs were mostly incurred by the health
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13
14 258 and aged care systems (£844.2 million), representing close to 1.5% of total
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16 259 expenditure on health and aged care in Australia. As many high-income western
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19 260 countries are dealing with issues of aging demographics and cognitive impairment,
20
21 261 our findings may be generalizable to other health and aged care systems. For
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23
24 262 example, previous research has found that delirium is associated with multiple
25
26 263 adverse outcomes including increased length and cost of hospitalization, functional
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28 264 and cognitive decline, institutionalization, and mortality.[2-4, 32] These results have
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30
31 265 significant implications for governments, who aim to identify conditions with high
32
33 266 social and financial costs for focused attention through public education and other
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35
36 267 initiatives that effect improvements in health status. The results of this study
37
38 268 highlight the need for concerted, worldwide efforts to mitigate the impacts of this
39
40
41 269 clinically significant and costly medical condition.
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43
44 270 There were 132,595 occurrences of delirium in Australia in 2016-17, but data from
45
46 271 the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity
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48
49 272 Database for 2015-16 indicate that as many as 1 in 5 cases are missed. This is
50
51 273 supported by previous research which suggests that delirium is undiagnosed in a
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54 274 large number of cases, ranging from approximately 25% of cases up to 87.5% in
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56 275 cases where dementia is also present.[11] This has significant implications for clinical
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3 276 practice as the outcomes of delirium are serious.[1] Future research could focus on
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5 277 techniques to improve the detection rate.
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9 278 Dementia represents a significant cost to the economy of all countries; the cost of
10
11 279 dementia due to delirium is therefore an important cost component of delirium. It
12
13 280 has been estimated that 47 million people are living with dementia globally, with
14
15 281 costs of £583 billion; moreover, prevalence is expected to triple over the next three
16
17 282 decades.[33] Overall, the costs of dementia attributable to delirium more than
18
19 283 doubled the total costs of delirium in Australia in 2016-17. We found that
20
21 284 approximately 10.6% of dementia cases, and thus costs, are associated with
22
23 285 delirium. Therefore, delirium imposes a large cost burden on residential aged care,
24
25 286 due to the high prevalence of dementia and the strong relationships between
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27 287 cognitive impairment and aged care. There may be considerable opportunities to
28
29 288 prevent some of the worldwide burden of dementia and improve the fiscal
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31 289 sustainability of health systems in the face of aging populations.
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38
39 290 Care for delirium following discharge from hospital relies heavily on informal carers,
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41 291 who provided almost 1 million hours of care to people with delirium. As workforce
42
43 292 participation increases and the propensity to care declines,[34] there is a risk that
44
45 293 the care needs of people with delirium will either go unmet, or require additional
46
47 294 government funding for aged care to meet their needs.
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50

51
52 295 There are some limitations to this study. First, the methods outlined the use of a
53
54 296 non-systematic search strategy, noting that this was fit-for-purpose when a number
55
56 297 of inputs were derived from official Australian Government statistics. The estimates
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3 298 presented should be interpreted with this in mind. Second, limited studies were
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6 299 found with appropriate methods to robustly estimate the prevalence of delirium in
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8 300 Australian hospital settings, but also in community or residential aged care settings.
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10 301 In order to minimize the impact of this limitation and the risk of double counting
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13 302 across studies, our analysis focused on delirium which met the full diagnostic criteria.
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15 303 Similarly, data paucity in some areas, such as out-of-hospital medical costs and
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17 304 productivity losses (employment outcomes) means that total estimates may be
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19
20 305 conservative. Given the methodology, the costs of delirium presented in this paper
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23 306 should be treated as an estimate only. More research, including observational
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25 307 studies in Australian settings, is required to understand the true costs incurred by
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27 308 people with delirium. However, a study that can capture costs across the health
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30 309 system and aged care settings in Australia will be technically challenging and may
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32 310 not be feasible due to the fragmented nature of the systems and data collection –
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35 311 particularly beyond the point at which people interact with the system. Finally, cost
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37 312 of illness studies provide guidance on the size of the problem, but are only useful for
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40 313 informing cost effective options for change when compared to the cost of such
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42 314 interventions. More work is needed to identify cost effective options to reduce the
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45 315 burden of delirium in Australia.

316 **CONCLUSION**

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

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3 320 with delirium and dementia. The financial costs of delirium were largely borne by
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6 321 Australian governments due to the health system and aged care expenditure.
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9 322 Further research should seek to understand the causes, treatment and prognosis of
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11 323 delirium, especially with regard to potential pathways from an episode of delirium to
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13 324 subsequent mortality outcomes and reduced cognitive functioning. Improving
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16 325 mortality outcomes and reducing decline in cognitive functioning would help to
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18 326 reduce the substantial financial and wellbeing costs of delirium.
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22 328 **Author contributions:**

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28 329 LP, JS and GC designed the study. JS and JH collected the data. All authors
29
30 330 contributed to the analysis and interpretation of the data. All authors read,
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32 331 commented on and approved the draft manuscript and reviewed the manuscript for
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34 332 important intellectual content. The sponsor was not directly involved in the findings
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36 333 of the research.
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41 334 **Conflicts of interest**

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44 335 The authors declare that they have no competing interests.
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53 338 **Patient and public involvement**

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56 339 Patient and public were not involved in this study.
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3 340 **Data sharing statement**
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6 341 No additional data are available.
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9 342 **FIGURE LEGENDS**
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13 343 Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £
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15 344 million.
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18 345 Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter
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20 346 inputs on the total cost of delirium in Australia in 2016 17.
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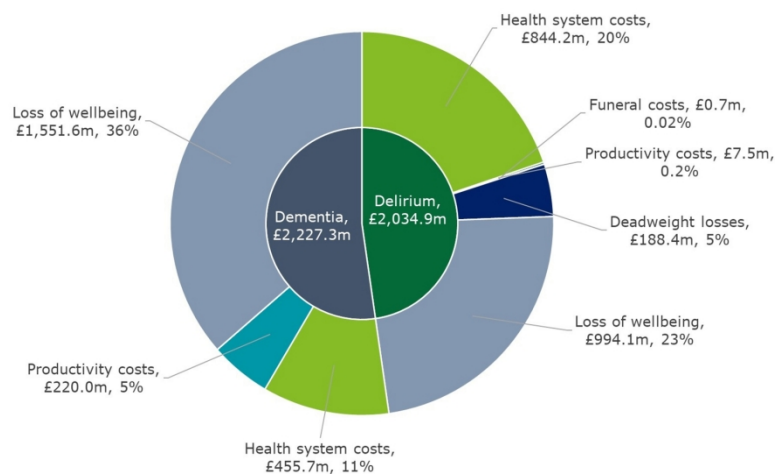


Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million

174x90mm (300 x 300 DPI)

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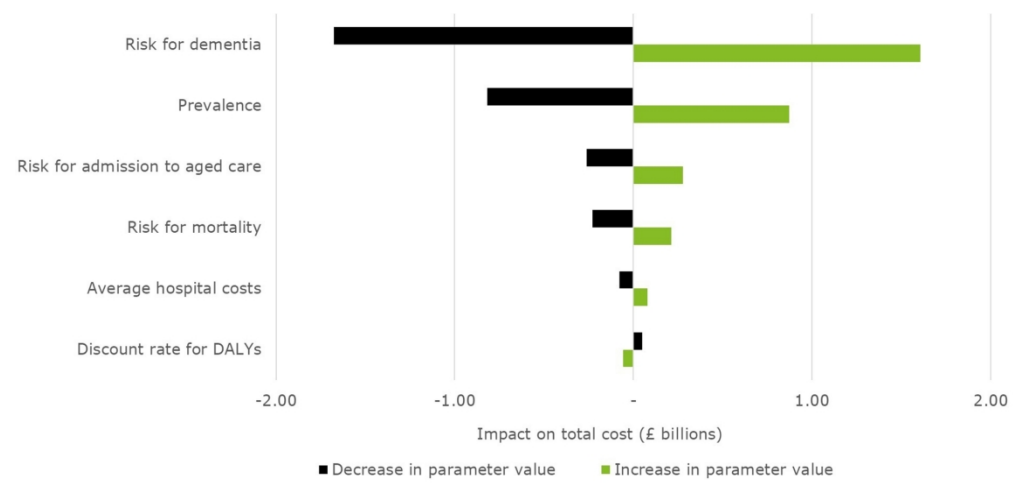


Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016-17

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

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3 **1 1 Epidemiology**

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2 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.

5 **1.1 Prevalence in episodes of acute hospital care**

6 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.

13 **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 al⁴						
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 al⁴ 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 al⁴ 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.

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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.

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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 Holmes²³), 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 al¹⁰). 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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67 **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
<i>Total</i>	<i>44,149</i>	<i>14,801</i>	<i>58,949</i>
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
<i>Total</i>	<i>42,393</i>	<i>31,253</i>	<i>73,646</i>
Total	86,541	46,054	132,595

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

69 **1.4 Duration of delirium episodes**

70 As delirium is a transient condition, it is important to estimate the average duration of an episode of
 71 delirium to calculate the burden imposed on society (Table 1.3).

72 **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

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

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74 **1.5 Mortality associated with delirium**

75 Delirium is associated with higher rates of mortality in hospital settings, and a greater chance of
 76 mortality occurring in the year following an episode of delirium. Mortality was estimated using an
 77 attributable fraction approach based on literature. Witlox et al³¹ reported an overall average
 78 mortality rate of 38.0% compared to a rate of 27.5% with no delirium, which was a 1.4-fold increase
 79 for those with delirium. The hazard ratio – indicating how much more likely someone with delirium
 80 is to have died at any point in time – was estimated to be 1.95. The authors included seven studies
 81 from the US, UK, Canada, Chile and Brazil. To estimate mortality associated with delirium for
 82 Australia, the Chilean and Brazilian studies have been excluded from the analysis as they are
 83 demographically less similar to Australia and there may be alternative drivers of mortality in those
 84 countries. The hazard ratio was re-estimated by meta-analysis using a random effects model. The
 85 final reweighted hazard ratio was estimated to be 1.77 (Table 1.5).

86 **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)

87 **Source:** Based on Witlox et al³¹

88 The hazard ratio (1.77) based on data from Witlox et al³¹ was applied to general population mortality
 89 rates, including the 1.4-fold increase for mortality for people who had delirium, for the respective
 90 age groups to estimate the number of deaths associated with delirium in 2016-17. It was expected
 91 that 12,571 people who had delirium would die in 2016-17, noting not all mortality is due to delirium
 92 itself (e.g. comorbid dementia or other illness may contribute to both delirium and death). Deaths

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3 93 due to delirium were estimated by applying the population attributable fraction to total deaths in
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5 94 the delirium cohort in 2016-17.^d
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^d The formula to estimate the number of deaths attributable to delirium is as follows:

$Population\ attributable\ fraction = \frac{P \cdot (HR - 1)}{P \cdot (HR - 1) + 1}$, 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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95 **2 Health and aged care system costs**96 **2.1 Hospital expenditure**

97 Hospital expenditure data in Australia includes general public and private hospital admissions. The
98 literature shows that delirium results in functional decline, resulting in a longer length of stay (LOS)
99 for hospital patients, consequently leading to higher hospitalisation expenditure. To estimate the
100 additional expenditure, the prevalence of delirium among hospitalised patients was applied to the
101 additional LOS and the average daily cost of care in a hospital setting.

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

105 The results of these studies were weighted by sample size to estimate the additional LOS for people
106 with delirium. On average, the LOS for people with delirium was estimated to be 24.2 days rather
107 than 16.7 days in the control groups, a difference of 7.5 days as shown in 0. The change in LOS is
108 similar to the average duration (5.9 days); however they may differ as people could develop an
109 episode of delirium either before or following hospital and have days with delirium outside of a
110 hospital setting.

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111 **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

112 Source: as itemised in table.

113 **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

114 Source: as itemised in table.

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

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

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3 121 • a secondary diagnosis, the average daily cost was adjusted to remove separation costs that were
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5 122 unlikely to be attributable to delirium, such as costs associated with surgery^f. The average daily
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7 123 cost for an additional separation was estimated to be \$1,329, which was applied to hospital
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9 124 prevalence as an additional diagnosis (106,098) and the additional LOS (2.7 days); and
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12 125 • a primary diagnosis (13,662 separations), the cost was assumed to be the same as the delirium
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14 126 diagnostic resource group, which was \$9,268 in 2016-17 after updating for inflation in the National
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16 127 Efficient Price.⁴²
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2.2 Out of hospital medical and other health professional expenditure

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24 130 There was limited evidence on the use of out of hospital medical and other health professional
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26 131 services in Australia. A study on psychosis related presentations to general practitioners (GPs)
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28 132 across Australia reported that 0.0175% of presentations were due to delirium,^g although no
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30 133 evidence was found for presentations to a specialist or other health professionals.⁴⁴ Consequently,
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32 134 cost estimates are only presented for GPs.

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36 135 The ratio of presentations to GPs was applied to Medicare Statistics data from the Department of
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38 136 Health's Summary Statistics by Broad Type of Service to estimate total GP consultations associated
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40 137 with delirium.⁴⁵ After adjusting for population growth, there were estimated to be 22,640 GP
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42 138 consultations associated with delirium in 2016-17.

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46 139 The average cost of a GP service was calculated based on Medicare Statistics data.⁴⁵ The average
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48 140 cost was derived using the total benefits provided for non-referred attendances (\$5.8 billion), the
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^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.

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3 141 number of services (129.37 million), the proportion of services which were bulk billed (83.7%), and
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5 142 the average out of pocket cost (\$33.38)^h.
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8 143 The average cost per consultation was estimated to be \$51.13 in 2016-17 terms. However, patients
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10 144 may present to GPs with more than one problem, and therefore the entire cost is not directly
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12 145 attributable to delirium. The average cost (\$51.13) was divided by the average number of problems
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14 146 (1.55) based on a report into General Practice Activity in Australia^{i,46}. The cost per consultation
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16 147 attributable to delirium was therefore estimated to be \$32.98 in 2016-17.
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20 148 **2.3 Residential aged care expenditure**

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22 149 Admission to residential aged care is a common outcome associated with delirium. A targeted
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24 150 literature review was conducted to estimate the likelihood of institutionalisation as a result of
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26 151 delirium. In a systematic review and meta-analysis of published studies that had controlled for
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28 152 confounding factors and illness severity, Witlox et al³¹ reported that people with delirium have a
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30 153 2.41 times greater chance of admission to aged care. The studies identified by Witlox et al³¹ are
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32 154 summarised in Table 2.4.
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59 ^h $(\text{Benefits} + (\text{Services} \times (1 - \frac{\text{Bulk billed rate}}{100})) \times \text{Out of pocket cost})$

60 ⁱ Britt et al⁴⁶ estimate an average number of problems of 1.55, total services were divided by this amount.

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155 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)

156 Source: Witlox et al³¹ Note: the average follow up across the studies was 14.6 months.

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

161 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

162 Source: as itemised in table.

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

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3 165 multiplied by the average cost of residential aged care. The number of admissions attributable to
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5 166 delirium was derived using the methods outlined in Eide and Heuch.^{50, j}
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8 167 The average cost was estimated using the Aged Care Financing Authority (ACFA's) 2016 Report on
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10 168 the Funding and Financing of Aged Care.⁵¹ The total expenditure on residential aged care services
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12 169 was \$14.9 billion in 2014-15, or \$90,793 per person in 2016-17 terms after dividing by the number of
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14 170 people in residential aged care and inflating to 2017 prices using the Consumer Price Index. The
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16 171 average cost per person was applied to the number of people admitted to residential aged care and
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18 172 adjusted by the total LOS, to arrive at the overall cost of residential aged care attributable to
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49 ^j First, the following two equations were solved simultaneously:

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

$$\frac{q1}{1-q1} * \frac{1-q2}{q2} = OR \quad (2)$$

51 where:

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

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

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

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174 **3 Other financial costs**175 **3.1 Absenteeism costs**

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

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

187 Average employment rates and average weekly earnings for people with delirium are based on ABS
188 data for the general population by age and gender.^{53;54} This was used for all productivity loss
189 calculations. From the literature, no studies could be located which estimated additional sick days
190 for people with delirium. As such, the estimated duration of delirium (5.9 days) was used to inform
191 time off work (assuming the person with delirium fully recovers before returning to work).

192 Absenteeism estimates will only occur for people with delirium who usually reside in a community
193 (as opposed to residential aged care) setting (prevalence of 86,541). Absenteeism costs were
194 estimated by applying the duration to the prevalence occurring in the working age population, and
195 adjusting for average employment rates and average weekly earnings.

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196 **3.2 Informal care costs**

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

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

208 Bellelli et al⁵⁵ found that 26.2% of patients who developed delirium during their hospital stay
209 required assistance from paid caregivers following discharge. The rate of paid caregiving was
210 assumed to be comparable to informal care in Australia as the care is usually provided by family
211 members. In order to estimate the number of care recipients for Australia, 26.2% was applied to the
212 prevalence of delirium for people who are 65 years or older and who live in the community (total
213 adjusted prevalence – prevalence in aged care). Therefore, it was estimated that 20,741 people
214 would require care due to delirium in Australia in 2016-17. People with delirium required assistance
215 with an additional 0.36 activities of daily living over a period of 12 months.^{56,57}

216 Analysis of the Survey of Disability, Ageing and Carers,⁵⁸ revealed an almost linear trend, such that
217 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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3 218 such, each person would receive 0.9 additional hours of care per week or 47.6 hours of care
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5 219 throughout the year.
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8 220 The carer's opportunity cost of time was calculated based on the weighted average weekly
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10 221 earnings⁵⁴ and the chance of being employed.⁵³
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222 **4 Dementia attributed to delirium**

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

- 227 • Lundstrom et al⁶⁰ estimated the odds ratio of developing new cases of dementia given delirium
228 was 5.66.
- 229 • Davis et al⁶¹ estimated the odds ratio of developing new cases of dementia given delirium was
230 8.65.
- 231 • Rockwood et al⁶² estimated the odds ratio of developing new dementia given delirium was 5.97.

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233 The sample for Davis et al was restricted to people over 85 years old, while Lundstrom et al and
234 Rockwood et al included people over 65 years old. The weighted odds ratio (based on sample size)
235 for people who are 65-84 years old was 5.88, while for people who are 85 years old or older, it was
236 estimated to be 7.56. Using the population attributable fraction approach outlined in Eide and
237 Heuch,⁵⁰ prevalence of delirium in our study and prevalence of dementia from Brown et al,⁶³ it was
238 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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1 **ABSTRACT**

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

4 Design, Setting and Participants: A cost of illness study was conducted for the
5 Australian population in the 2016-17 financial year. The prevalence of delirium in
6 2016-17 was calculated to inform cost estimations. The costs estimated in this study
7 also include dementia attributable to delirium.

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

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

18 Dementia attributable to delirium accounted for £2.2 billion of the total cost of
19 delirium.

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

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3 23 and cognitive decline associated with delirium and dementia. To reduce the
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5 24 substantial wellbeing costs of delirium, further research should seek to better
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8 25 understand the potential pathways from an episode of delirium to subsequent
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10 26 mortality and reduced cognitive functioning outcomes.
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16 28 **Strengths and limitations of this study**

- 19 29 • This cost of illness study estimates the total annual financial and wellbeing
20 30 impacts of delirium for the first time in Australia.
- 21 31 • This study also estimates the costs of dementia that are associated with delirium
22 32 in Australia, with significant implications for other high income western
23 33 countries.
- 24 34 • This study is based on non-systematic search strategy to find relevant cost
25 35 inputs, noting that a number of inputs are sourced from official Australian
26 36 Government statistics.
- 27 37 • There were a number of data gaps when estimating costs, meaning the results of
28 38 our study are only indicative of the total cost.
- 29 39 • Cost of illness studies provide guidance on the size of the problem, but more
30 40 work is need to identify cost effective interventions to reduce the burden of
31 41 delirium.

42 INTRODUCTION

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

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

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3 63 A previous study in the United States, undertaken over a decade ago, assessed the
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6 64 costs associated with delirium after adjusting for patient sociodemographic and
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8 65 clinical characteristics and found that hospital costs per day for patients with
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10 66 delirium were more than double the costs of patients who did not experience an
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13 67 episode of delirium.[9] Additionally, previous studies have found associations
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15 68 between delirium and long-term cognitive impairment and dementia,[10] and
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17 69 premature death.[3, 11] However, the relative costs of these outcomes have not yet
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20 70 been established.

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23 71 To date, no studies have estimated the costs of delirium in Australia. Understanding
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25
26 72 the costs of delirium is important because delirium is often missed in as many as two
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28 73 thirds of cases,[12] although there are validated tools for diagnosing delirium such as
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30 74 the Confusion Assessment Method.[2] By better understanding the costs, morbidity
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32
33 75 and mortality of delirium, it is possible to answer the question of whether it would
34
35 76 be worthwhile to pay more attention to its prevention, diagnosis and treatment.
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38 77 Different costs of disease are borne by different individuals or sectors of society.
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41 78 Understanding how the costs are shared helps to make informed decisions regarding
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43 79 interventions. The purpose of this study was to raise awareness of the impacts of
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46 80 delirium and contribute to improving policy in this area, by quantifying the
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48 81 magnitude of the economic burden associated with delirium in Australia in 2016-17.

51 82 **METHODS**

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55 83 In this study, the financial costs of delirium to the Australian health system include
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57 84 the costs of running hospitals and nursing homes, GP and specialist services
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3 85 reimbursed through Australia's universal health insurance scheme and private funds,
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6 86 the cost of pharmaceuticals and over-the-counter medications, allied health services,
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8 87 research and health administration. The other financial costs of delirium in this study
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10 88 include productivity costs, the cost of informal care, funeral costs, and deadweight
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13 89 losses associated with taxation payments and administration. The loss of wellbeing
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15 90 due to delirium was measured using disability adjusted life years (DALYs).
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18 91 **Prevalence**

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21 92 This cost of illness study was conducted using standard methodology,[13] based on a
22
23 93 prevalence approach to cost measurement. Prevalence approaches measure the
24
25 94 number of people with a given condition in a base period and the costs associated
26
27 95 with treating them, as well as other financial and non-financial costs in that year due
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29 96 to the condition. This approach is combined with both bottom-up and top-down
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31 97 approaches to estimate expenditure for each cost component.[13] For example, a
32
33 98 top-down approach has been used to estimate the costs of dementia due to
34
35 99 delirium, while most costs of delirium have been established using a bottom-up
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37 100 approach. The methodology is consistent with previously published research in this
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39 101 field in Australia and internationally.[14-16] Costs were estimated from the
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41 102 perspective of Australian society for the 2016-17 financial year.
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49 103 A targeted literature review was conducted to identify the prevalence of delirium in
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51 104 acute hospitalizations, nursing homes and in the community (without presenting to
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53 105 hospital). The targeted review was investigative in nature and considered fit-for-
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55 106 purpose as the prevalence and methods vary widely across studies. The focus of the
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3 107 literature review was on prevalence in a hospital setting. For hospitalizations, studies
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5 108 were included if they provided results for general medical or surgical wards (i.e. an
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8 109 acute setting) for the duration of the hospital stay using validated diagnostic
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11 110 measures. Results from the literature searches were pooled by taking a weighted
12
13 111 average to estimate an average prevalence that could be applied to Australian
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15 112 hospital separations (Additional File 1, Table 1). Overall, the prevalence of delirium in
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17 113 a hospital setting was estimated to be 20.2% on average, which was applied to the
18
19 114 521,099 overnight acute emergency hospital separations for people aged 70 years or
20
21 115 older in 2016-17.[17] Therefore, there were approximately 105,182 hospital
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23 116 separations involving delirium in 2016-17, of which delirium was recorded as the
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25 117 principal diagnosis for approximately 11,999 separations in 2016-17.[18]
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29 118 Additional diagnosis separations in younger age groups (less than 70 years old) were
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31 119 estimated by applying the ratio between total and principal delirium diagnoses to
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33 120 principal diagnoses in the younger age groups. [17,18] We estimate there were
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35 121 14,578 separations for younger Australians, and 119,760 total cases of delirium in
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37 122 Australian hospitals in 2016-17.
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43 123 No prevalence studies in Australian nursing homes were identified. Prevalence
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45 124 results were thus derived from a study from the Netherlands,[19] due to similarities
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47 125 in aged care settings, demographic profiles and medication prescribing rates – for
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49 126 example, both countries exhibit high rates of psychotropic medication prescribing
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51 127 (though there are some differences in the preferred antipsychotic agent),[20]
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53 128 despite their limited efficacy and adverse effects in people with delirium.[7] The
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55 129 combined prevalence and incidence was 8.5% and 16.9 per 100 person-years
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3 130 respectively. These rates are similar to the rates reported in other international
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6 131 literature.[21-23]
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9 132 In Australia on 30 June 2015, there were 172,044 permanent residents in aged care
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11 133 facilities. Using estimated population growth by age group from the Australian
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13 134 Bureau of Statistics (ABS),[24] we estimate there would have been 181,314
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16 135 permanent residents in Australian aged care facilities on 30 June 2017. Applying the
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18 136 prevalence (at baseline), and the incidence per 100 person years from Boorsma et
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20
21 137 al,[19] we estimate that 46,054 permanent residents had delirium in 2016-17.
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24 138 The total prevalence of delirium in Australia 2016-17 was adjusted to avoid double
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26 139 counting people in the residential aged care cohort who also present to hospital. The
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28 140 following rates were used to adjust the prevalence to avoid double counting people
29
30 141 in residential aged care who also present to hospital: 50% of cases were delirious at
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32 142 admission;[25] 43% of hospitalized patients were delirious at discharge;[26] 31.2%
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34 143 were admitted from residential aged care while 68.9% were admitted from the
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36 144 community;[27] and of people with delirium, 28% of patients were discharged to
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38 145 residential aged care, 63% were discharged to the community, and 9% died before
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40 146 discharge from hospital.[28]
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45 46 47 147 **Average duration of an episode of delirium and mortality**

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49 148 A targeted literature review was conducted to identify studies that reported the
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51 149 average duration of delirium across hospital and residential aged care settings. The
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53 150 average duration of delirium was estimated by taking a weighted average of the
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3 151 findings reported in twelve studies (Additional File 1, Table 2), which was 5.9 days on
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6 152 average.

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9 153 Mortality associated with delirium was estimated using an attributable fraction
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11 154 approach,[13] and the hazard ratio of 1.77 used in our analysis was based on a
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13 155 previous systematic review and meta-analysis (Additional File 1, Table 3).[3]. The
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16 156 hazard ratio was used to estimate an attributable fraction for how many deaths are
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18 157 due to delirium in Australia.

21 158 **Health care system expenditure**

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25 159 A targeted literature review was conducted to identify studies that reported cost
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27 160 inputs suitable to estimate health care system expenditure. The review was
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30 161 considered more fit-for-purpose than a systematic review given this was a cost of
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32 162 illness study where many of the inputs are in data sets and grey literature (e.g.
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34 163 government documents), not in peer-reviewed literature.

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37 164 Health system costs were estimated using a bottom-up approach. This includes costs
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40 165 associated with hospital, medication, and research expenditure, out of hospital
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42 166 medical and other health professionals' expenditure, and residential aged care
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45 167 expenditure. Delirium induces functional decline, resulting in a longer length of stay
46
47 168 (LOS) for older people in hospital, consequently leading to higher hospitalization
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50 169 expenditure.[2] To estimate the additional expenditure, the prevalence of delirium
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52 170 among hospitalized older people was applied to the additional LOS and the average
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55 171 daily cost of care in a hospital setting.

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3 172 The average daily cost of an acute separation was obtained from the Independent
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5 173 Hospital Pricing Authority (IHPA) for 2014-15 and adjusted by the standard index
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8 174 rate used by IHPA (2.1%) to estimate the cost for the 2016-17 base year.[29] The
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10 175 average cost of any separation for 2016-17 was estimated to be £2,538, or £961 per
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12 176 day in 2016-17 terms. The average daily cost was also adjusted by an additional
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14 177 14.3% to inflate for non-allocated health costs (an allowance for capital costs) based
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16 178 on AIHW.[30] Where delirium was a secondary diagnosis, the average daily cost was
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18 179 adjusted to remove separation costs that were unlikely to be attributable to
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20 180 delirium, such as costs associated with surgery. The average daily cost for an
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22 181 additional separation was estimated to be £644, which was applied to hospital
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24 182 prevalence as an additional diagnosis (106,098) and the additional LOS due to
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26 183 delirium, which was assumed to be 2.7 days (see Additional File 1, Table 4 and
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28 184 Additional File 1, Table 5). Where delirium was a primary diagnosis (13,662
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30 185 separations), the cost was assumed to be the same as the delirium diagnostic
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32 186 resource group, which was £4,489 in 2016-17 after updating for inflation in the
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34 187 National Efficient Price.[29]
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37 188 To estimate health research expenditure on delirium in Australia in 2016-17, this
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39 189 report utilized the National Health and Medical Research Council (NHMRC) grants
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41 190 database. The database outlines all NHMRC research grant funding between 2000
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43 191 and 2016 and provides a description of the projects and key outcomes achieved.[31]
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45 192 Annual funding allocated to delirium research in 2016-17 was estimated by taking an
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47 193 average across the historical years. Other forms of health research where research
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3 194 costs can be recovered – for example, by charging a higher price for services – were
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6 195 not considered in this analysis, consistent with standard methodology.[13]
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9 196 Out of hospital medical expenditure (GP consultations) was estimated by applying
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11 197 the average cost per GP consultation (approximately £16 after adjusting for multiple
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13 198 problems per GP consultation),[32] to the total services associated with organic
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16 199 psychoses in Australia,[33] which was considered comparable to delirium. After
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18 200 adjusting for population growth, there were estimated to be 22,640 GP consultations
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21 201 associated with delirium in 2016-17.

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24 202 Residential aged care expenditure was estimated using an attributable fraction
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26 203 approach based on literature to estimate admissions to aged care due to cognitive
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28 204 decline associated with delirium. The odds ratio for admission (2.41),[4] was
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30
31 205 converted to an attributable fraction. The number of admissions was adjusted by
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33 206 average LOS in residential aged care in Australia and applied to the average costs
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36 207 associated with residential aged care, which was estimated to be £43,978 per person
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38
39 208 based on the total expenditure on residential aged care services in Australia.[34]

40 41 42 209 **Other financial costs**

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44
45 210 The economic cost of short run productivity losses associated with absenteeism
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47 211 were estimated using the friction cost method.[13] Average employment rates and
48
49 212 average weekly earnings for people with delirium are based on ABS data for the
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51
52 213 general population by age and gender.[35, 36] Absenteeism was estimated as the
53
54 214 duration of delirium (5.9 days) for separations that occur in the working age
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57 215 population, adjusted for employment rates.

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3 216 Carers are people who provide care to others in need of assistance or support. An
4
5 217 informal carer provides this service without formal payment and does so outside of
6
7 218 the formal care sector. On average, we estimate that each person with delirium
8
9 219 would have received an additional 0.9 hours of care per week, based on the change
10
11 220 in activities of daily living over a period of 12 months (Additional File 1 provides
12
13 221 supplementary information that was used to estimate the additional hours of
14
15 222 care).[37, 38] The dollar value of informal care was estimated as the opportunity
16
17 223 cost of a carer's time, which was based on general population average weekly
18
19 224 earnings and employment rates.[35, 36]
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21 225 The additional cost of funerals borne by family and friends of people with delirium
22
23 226 was based on the number of deaths associated with delirium. The cost of a funeral
24
25 227 was assumed to be £4,602. Funeral costs were brought forward by the average life
26
27 228 expectancy at age of death. The deadweight losses due to lost taxation revenue
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29 229 (given an assumption of no change in spending) and additional government spending
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31 230 on delirium was calculated by applying the average marginal excess burden of
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33 231 taxation of £0.31 per £1 of tax.[39, 40]
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232 **Loss of wellbeing**

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46 233 Burden of disease methodology was employed to quantify the impact of delirium on
47
48 234 wellbeing.[41] The approach is non-financial, where pain, suffering and premature
49
50 235 mortality are measured in terms of disability adjusted life years (DALYs). DALYs are
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52 236 comprised of years of healthy life lost due to morbidity (YLDs) and years of life lost
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54 237 due to premature mortality (YLLs).[41] YLDs were calculated using a prevalence
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3 238 approach, whereby the disability weight was multiplied by average duration of
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5 239 delirium. The disability weight for delirium used in this study was 0.17.[42] Duration
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7
8 240 of delirium was based on the prevalence of persistent delirium over 12 months.[43]
9
10 241 DALYs were converted to a monetary value using the value of a statistical life year
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12 242 (£93,882), which is an official estimate updated for inflation using the Consumer
13
14 243 Price Index.[44] The value of a statistical life year was discounted at a rate of 3% per
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16 244 annum where it has been applied to future years of life lost due to morality from
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18 245 delirium.
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23 246 **Costs of dementia attributable to delirium**

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26 247 Costs of dementia were sourced from an Australian cost of illness study.[45] Inputs
27
28 248 were taken for Australia in the 2016 financial year, and updated using either health
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30 249 inflation or the Consumer Price Index as appropriate. The wellbeing cost attributable
31
32 250 to dementia for YLLs or YLDs was estimated using data from the Australian Institute
33
34 251 of Health and Welfare's Australian Burden of Disease Study.[46] The proportion of
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36 252 dementia attributable to delirium was estimated using the population attributable
37
38 253 fraction approach. The odds ratio for developing a new case was 5.88 for people
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40 254 aged 65-84 years old and 7.56 for people aged 85 years or older,[47-49] which was
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42 255 used to estimate an attributable fraction.
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49 256 **Sensitivity analysis**

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52 257 One-way sensitivity analyses were conducted on prevalence, the risk for mortality,
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54 258 dementia admission to aged care, average hospital costs, discount rate for DALYs,
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56 259 and the value of a statistical life year. The specific values represent the upper and
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3 260 lower 95% confidence intervals for the relevant input parameters where available, or
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6 261 unit costs that were 25% higher or lower if the distribution was unknown.
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9 262 **Currency standardization**

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11 263 All costs are expressed in 2016-17 pound sterling. Costs were converted from
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13 264 Australian dollars using the 2017 Organisation for Economic Cooperation and
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16 265 Development purchasing power parity of 2.065 Australian dollars per pound sterling
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19 266 in 2017.[50]
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22 267 **Data analysis and ethical considerations**

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25 268 Data for this study was collected throughout January to June 2017 by the authors
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27
28 269 from a range of public data sources and literature. The data was analyzed and
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30 270 compiled in Microsoft Excel. No individual patient data was collected for the study
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33 271 and therefore, this study did not require ethics approval.
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36 272 **Patient and public involvement**

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39 273 Patient and public were not involved in this study.
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42 274 **RESULTS**

43 44 45 275 **Prevalence and mortality**

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48 276 There were an estimated 132,595 cases of delirium in Australia in 2016-17,
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51 277 representing both cases that occur in hospital and aged care. This is equivalent to
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53 278 approximately 0.5% of the population in Australia, although some individuals may
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56 279 experience delirium more than once in a year. Prevalence by age and gender are
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59 280 available in Table 1. The rates increase substantially with age.
60

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

<i>Age/ gender</i>	<i>Community</i>	<i>Residential aged care</i>	<i>Total</i>	<i>% of general population</i>
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
<i>Total</i>	<i>44,149</i>	<i>14,801</i>	<i>58,949</i>	<i>0.5</i>
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
<i>Total</i>	<i>42,393</i>	<i>31,253</i>	<i>73,646</i>	<i>0.6</i>
Person	86,541	46,054	132,595	0.5

282

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

286 Health care system expenditure

287 Delirium most commonly occurred in hospitals, with an estimated 119,760 cases
 288 (some of these individuals usually reside in aged care). Total health system and aged
 289 care costs associated with delirium in Australia were estimated to be £844.2 million
 290 in 2016-17. The total comprised hospital (£247.3 million), residential aged care
 291 (£596.2 million), out-of-hospital medical (£0.4 million), and research expenditure
 292 (£0.3 million).

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3 293 **Other financial costs**
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6 294 Other financial costs – including absenteeism costs (£6.6 million), informal care costs
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8 295 (£0.8 million), brought forward funeral costs (£0.7 million) and deadweight losses
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10 296 (£188.4 million) – for people with delirium were estimated to be £196.6 million in
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12 297 Australia in 2016-17. Productivity losses imposed by delirium were estimated to be
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14 298 relatively small. The cost of informal care (£0.8 million) was relatively small due to
15
16 299 the low opportunity cost of carer time (£0.84 per hour); informal carers provided
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18 300 987,958 hours of care.
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24 301 **Loss of wellbeing**
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27 302 The total burden of disease from delirium in 2016-17 was estimated to be
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29 303 £994.1 million. Overall, people with delirium experienced: 5,441 years of healthy life
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31 304 lost due to disability (YLDs), or 0.041 YLDs per person with delirium; 5,687 years of
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33 305 life lost due to premature death (YLLs), or 0.043 YLLs per person with delirium; and
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35 306 11,128 DALYs overall, or around 0.084 DALYs per person with delirium in 2016-17.
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40 307 **Costs of dementia attributable to delirium**
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43 308 Overall, it was estimated that 40,981 or 10.6% cases of dementia were attributable
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45 309 to delirium, which largely occur in people aged 85 years or older. The total costs of
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47 310 dementia due to delirium were estimated to be £2.2 billion, of which the financial
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49 311 costs were £675.7 million and the loss of wellbeing was £1.6 billion. Table 2 shows
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51 312 cost breakdowns by age and gender group. Figure 1 shows the costs of dementia due
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53 313 to delirium broken down by health system and aged care costs, other financial costs
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55 314 and burden of disease.
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315 Table 2. Costs of delirium in Australia in 2016-17, by age and gender group, £ million
316 or %

<i>Age/ gender</i>	<i>Financial cost</i>		<i>Wellbeing cost</i>		<i>Total</i>	<i>% of total</i>
	<i>Delirium</i>	<i>Dementia due to delirium</i>	<i>Delirium</i>	<i>Dementia due to delirium</i>		
Male						
<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	

317

318 (INSERT FIGURE 1)

319 Total costs

320 The total costs of delirium in Australia were estimated to be £4.3 billion

321 (AUD8.8 billion) in 2016-17. The total cost comprised financial costs of £1.7 billion

322 (AUD3.5 billion) and the value of healthy life lost of £2.5 billion (AUD5.3 billion).

323 Table 3 shows the costs of delirium broken down by health system and aged care

324 costs, other financial costs, and burden of disease.

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

<i>Cost component</i>	<i>Total (£ million)</i>	<i>Per person with delirium (£)</i>
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

326

327 **Sensitivity analysis**

328 The results and specific values for the sensitivity analysis are shown in Table 4 and

329 Figure 2. The total cost of delirium in Australia was most sensitive to changes in the

330 risk for dementia following delirium and the overall prevalence rate. The total cost of

331 delirium was estimated to range from £2.6 billion to £5.9 billion in Australia in

332 2016-17.

333 Table 4. Sensitivity analysis, £ million

<i>Variable</i>	<i>Financial</i>	<i>Loss of wellbeing</i>	<i>Total</i>
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

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

335

336 (INSERT FIGURE 2)

337 DISCUSSION

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

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3 343 is critical that such economic estimations are undertaken as they inform decision
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6 344 making.

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9 345 According to our findings, delirium imposes a substantial burden on society.
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11 346 Considering delirium alone, the economic costs were mostly incurred by the health
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13 347 and aged care systems (£844.2 million), representing close to 1.5% of total
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16 348 expenditure on health and aged care in Australia. As many high-income western
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18 349 countries are dealing with issues of aging demographics and cognitive impairment,
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21 350 our findings may be generalizable to other health and aged care systems. For
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23 351 example, previous research has found that delirium is associated with multiple
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26 352 adverse outcomes including increased length and cost of hospitalization, functional
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28 353 and cognitive decline, institutionalization, and mortality.[2-5, 51] These results have
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30
31 354 significant implications for governments, who aim to identify conditions with high
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33 355 social and financial costs for focused attention through public education and other
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36 356 initiatives that effect improvements in health status. The results of this study
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38 357 highlight the need for concerted, worldwide efforts to mitigate the impacts of this
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41 358 clinically significant and costly medical condition.

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44 359 According to our estimates, there were 132,595 occurrences of delirium in Australia
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46 360 in 2016-17, but data from the Australian Institute of Health and Welfare National
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48 361 Hospital Morbidity Database for 2015-16 indicate that as many as 1 in 5 cases are
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51 362 missed. This is supported by previous research which suggests that delirium is
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53 363 undiagnosed in a large number of cases, ranging from approximately 25% of cases up
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56 364 to 87.5% in cases where dementia is also present.[12] This has significant

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3 365 implications for clinical practice as the outcomes of delirium are serious.[1] Future
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5 366 research could focus on techniques to improve the detection rate.
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9 367 Dementia represents a significant cost to the economy of all countries; the cost of
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11 368 dementia due to delirium is therefore an important cost component of delirium. It
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13 369 has been estimated that 47 million people are living with dementia globally, with
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15 370 costs of £583 billion; moreover, prevalence is expected to triple over the next three
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17 371 decades.[52] Overall, the costs of dementia attributable to delirium more than
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19 372 doubled the total costs of delirium in Australia in 2016-17. We found that
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21 373 approximately 10.6% of dementia cases, and thus costs, are associated with
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23 374 delirium. Therefore, delirium imposes a large cost burden on residential aged care,
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25 375 due to the high prevalence of dementia and the strong relationships between
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27 376 cognitive impairment and aged care. There may be considerable opportunities to
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29 377 prevent some of the worldwide burden of dementia and improve the fiscal
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31 378 sustainability of health systems in the face of aging populations.
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39 379 Care for delirium following discharge from hospital relies heavily on informal carers,
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41 380 who provided almost 1 million hours of care to people with delirium. As workforce
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43 381 participation increases and the propensity to care declines,[53] there is a risk that
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45 382 the care needs of people with delirium will either go unmet, or require additional
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47 383 government funding for aged care to meet their needs.
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51 384 There are some limitations to this study. First, the methods outlined the use of a
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53 385 non-systematic search strategy, noting that this was fit-for-purpose when a number
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55 386 of inputs were derived from official Australian Government statistics. The estimates
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3 387 presented should be interpreted with this in mind. Second, limited studies were
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6 388 found with appropriate methods to robustly estimate the prevalence of delirium in
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8 389 Australian hospital settings, but also in community or residential aged care settings.
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10 390 In order to minimize the impact of this limitation and the risk of double counting
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13 391 across studies, our analysis focused on delirium which met the full diagnostic criteria.
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15 392 Similarly, data paucity in some areas, such as out-of-hospital medical costs and
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18 393 productivity losses (employment outcomes) means that total estimates may be
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20 394 conservative. Given the methodology, the costs of delirium presented in this paper
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23 395 should be treated as an estimate only. More research, including observational
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25 396 studies in Australian settings, is required to understand the true costs incurred by
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28 397 people with delirium. However, a study that can capture costs across the health
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30 398 system and aged care settings in Australia will be technically challenging and may
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33 399 not be feasible due to the fragmented nature of the systems and data collection –
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35 400 particularly beyond the point at which people interact with the system. Finally, cost
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38 401 of illness studies provide guidance on the size of the problem, but are only useful for
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40 402 informing cost effective options for change when compared to the cost of such
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43 403 interventions. More work is needed to identify cost effective options to reduce the
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45 404 burden of delirium in Australia.

48 405 **CONCLUSION**

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51 406 In summary, delirium imposes a substantial burden on Australian society – both in
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54 407 terms of financial costs associated with health system expenditure and a greater
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57 408 need for residential aged care due to the functional and cognitive decline associated
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3 409 with delirium and dementia. The financial costs of delirium were largely borne by
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6 410 Australian governments due to the health system and aged care expenditure.
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9 411 Further research should seek to understand the causes, treatment and prognosis of
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11 412 delirium, especially with regard to potential pathways from an episode of delirium to
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13 413 subsequent mortality outcomes and reduced cognitive functioning. Improving
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16 414 mortality outcomes and reducing decline in cognitive functioning would help to
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19 415 reduce the substantial financial and wellbeing costs of delirium.
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22 417 **Author contributions:**

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27
28 418 LP, JS and GC conceived of and designed the study. JS, JH and LP collated the data,
29
30 419 performed the data analysis and contributed to interpretation and reporting of the
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32
33 420 data. AT, MA and GC contributed to the interpretation and reporting of the data. All
34
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36 421 authors read, commented on and approved the final manuscript, and all authors
37
38 422 reviewed the manuscript for important intellectual content. The sponsor was not
39
40
41 423 directly involved in the findings of the research.
42

43 424 **Conflicts of interest**

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45
46 425 The authors declare that they have no competing interests.
47
48

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50
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52 427 The research was supported by the Australasian Delirium Association.
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55 428 **Data sharing statement**

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3 429 No additional data are available.
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6 430 **FIGURE LEGENDS**
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10 431 Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £
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12 432 million.
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15 433 Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter
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17 434 inputs on the total cost of delirium in Australia in 2016 17.
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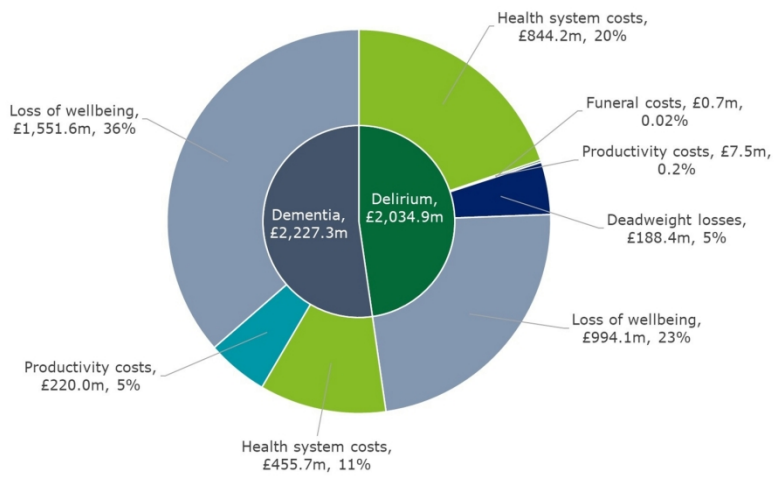


Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million

174x90mm (300 x 300 DPI)

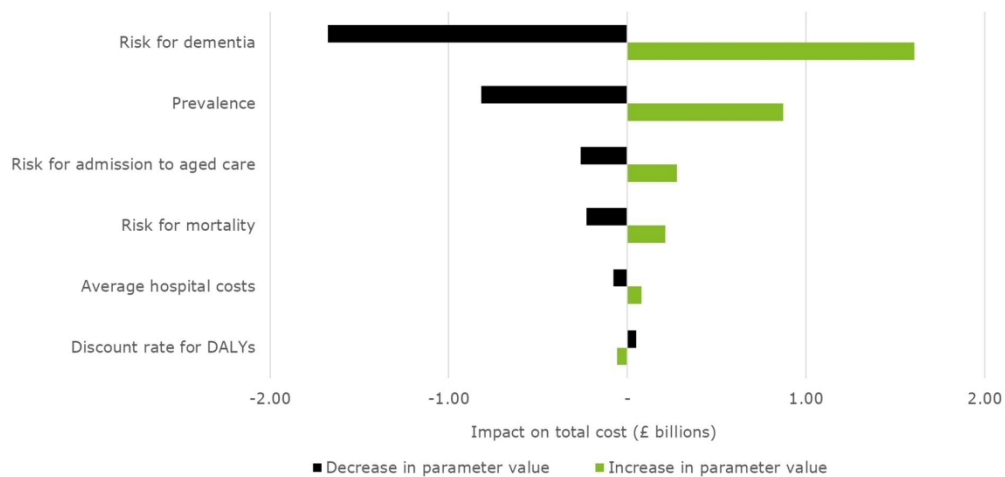


Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016-17

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

1	1	1	CHEERS checklist	2
2	2	2	Literature review strategy	4
3	3	3	Epidemiology	5
4	4	3.1	Prevalence in episodes of acute hospital care	5
5	5	3.2	Duration of delirium episodes.....	6
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For peer review only

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

10 1 CHEERS checklist

11 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	<i>Single study-based estimates:</i> 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	<i>Synthesis-based estimates:</i> 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	<i>Single study-based economic evaluation:</i> 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	<i>Model-based economic evaluation:</i> 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.

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

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	<i>Single study-based economic evaluation:</i> 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	<i>Model-based economic evaluation:</i> 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.

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

12 **2 Literature review strategy**

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

- 18 1. ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]) AND Meta-
19 Analysis[ptyp].
- 20 2. ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]) AND
21 "Australia"[pl].
- 22 3. ("epidemiology"[MH] OR "mortality"[MH] OR "incidence"[MH] OR "prevalence"[MH] OR
23 "duration"[tiab] OR "persistence"[tiab]) AND ("delirium"[tiab] OR "cognitive
24 impairment"[tiab] OR "acute confusion"[tiab])).
- 25 4. 3 AND "Australia"[pl].
- 26 5. 3 AND "Australia"[pl] AND ("hospital"[tiab] OR "aged care"[tiab] OR "nursing home"[tiab]).
- 27 6. ("cost"[tiab] OR "economic"[tiab] OR "productivity"[tiab] OR "workforce"[tiab] OR "health
28 use"[tiab] OR "utilization"[tiab]) AND ("delirium"[tiab] OR "cognitive impairment"[tiab] OR
29 "acute confusion"[tiab]).
- 30 7. 5 and "Australia"[pl].
- 31 8. ("burden"[tiab] OR "disability"[tiab] OR "death"[tiab] OR "quality of life"[tiab]) AND
32 ("delirium"[tiab] OR "cognitive impairment"[tiab] OR "acute confusion"[tiab]).
- 33 9. 7 AND "Australia"[pl].

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

34 **3 Epidemiology**

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

38 **3.1 Prevalence in episodes of acute hospital care**

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

42 **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 al¹						
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 al¹ 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

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

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
Iseki 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 al¹ 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.

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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 al²² 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 al²²

The hazard ratio (1.77) based on data from Witlox et al²² 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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3 68 due to delirium were estimated by applying the population attributable fraction to total deaths in
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5 69 the delirium cohort in 2016-17.^b
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^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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70 **4 Hospital expenditure**

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

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

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

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84 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

85 Source: as itemised in table.

86 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

87 Source: as itemised in table.

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88 **5 Informal care costs**

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

93 Bellelli et al³³ found that 26.2% of patients who developed delirium during their hospital stay
94 required assistance from paid caregivers following discharge. The rate of paid caregiving was
95 assumed to be comparable to informal care in Australia as the care is usually provided by family
96 members. In order to estimate the number of care recipients for Australia, 26.2% was applied to the
97 prevalence of delirium for people who are 65 years or older and who live in the community (total
98 adjusted prevalence – prevalence in aged care). Therefore, it was estimated that 20,741 people
99 would require care due to delirium in Australia in 2016-17. People with delirium required assistance
100 with an additional 0.36 activities of daily living over a period of 12 months.^{34,35}

101 Analysis of the Survey of Disability, Ageing and Carers,³⁶ revealed an almost linear trend, such that
102 an additional 2.57 hours of care were provided per week for each additional activity on average.^c As
103 such, each person would receive 0.9 additional hours of care per week or 47.6 hours of care
104 throughout the year.

105 The carer's opportunity cost of time was calculated based on the weighted average weekly
106 earnings³⁷ 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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The economic impact of delirium in Australia: a cost of illness study

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1 **ABSTRACT**

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

4 Design, Setting and Participants: A cost of illness study was conducted for the
5 Australian population in the 2016-17 financial year. The prevalence of delirium in
6 2016-17 was calculated to inform cost estimations. The costs estimated in this study
7 also include dementia attributable to delirium.

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

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

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

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3 23 and cognitive decline associated with delirium and dementia. To reduce the
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5 24 substantial wellbeing costs of delirium, further research should seek to better
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8 25 understand the potential pathways from an episode of delirium to subsequent
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10 26 mortality and reduced cognitive functioning outcomes.
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16 28 **Strengths and limitations of this study**

- 19 29 • This cost of illness study estimates the total annual financial and wellbeing
20 30 impacts of delirium for the first time in Australia.
- 21 31 • This study also estimates the costs of dementia that are associated with delirium
22 32 in Australia, with significant implications for other high income western
23 33 countries.
- 24 34 • This study is based on a non-systematic search strategy to find relevant cost
25 35 inputs, noting that a number of inputs are sourced from official Australian
26 36 Government statistics.
- 27 37 • There were a number of data gaps when estimating costs, meaning the results of
28 38 this study are only indicative of the total cost.
- 29 39 • While this cost of illness study estimates the overall cost of delirium, more work
30 40 is needed to identify cost effective interventions to reduce the burden of
31 41 delirium.

42 INTRODUCTION

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

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

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3 63 A previous study in the United States, undertaken over a decade ago, assessed the
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6 64 costs associated with delirium after adjusting for patient sociodemographic and
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8 65 clinical characteristics and found that hospital costs per day for patients with
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10 66 delirium were more than double the costs of patients who did not experience an
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13 67 episode of delirium.[9] Additionally, previous studies have found associations
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15 68 between delirium and long-term cognitive impairment and dementia,[10] and
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17 69 premature death.[3, 11] However, the relative costs of these outcomes have not yet
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20 70 been established.

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23 71 To date, no studies have estimated the costs of delirium in Australia. Understanding
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25 72 the costs of delirium is important because delirium is often missed in as many as two
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27 73 thirds of cases,[12] although there are validated tools for diagnosing delirium such as
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29 74 the Confusion Assessment Method.[2]

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33 75 By better understanding the costs, morbidity and mortality of delirium, it is possible
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35 76 to answer the question of whether it would be worthwhile to pay more attention to
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37 77 its prevention and diagnosis. Understanding the costs of delirium also helps to make
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39 78 informed decisions regarding treatment interventions. The purpose of this study was
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41 79 to raise awareness of the impacts of delirium and contribute to improving policy in
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43 80 this area, by quantifying the magnitude of the economic burden associated with
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45 81 delirium in Australia in 2016-17.

51 82 **METHODS**

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55 83 This cost of illness study was conducted using standard methodology,[13] based on a
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57 84 prevalence approach to cost measurement. Prevalence approaches measure the

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3 85 number of people with a given condition in a base period and the costs associated
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5 86 with treating them, as well as other financial and non-financial costs in that year due
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8 87 to the condition. This approach was combined with both bottom-up and top-down
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10 88 approaches to estimate expenditure for each cost component.[13] For example, a
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13 89 top-down approach was used to estimate the costs of dementia due to delirium,
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15 90 while most costs of delirium have been established using a bottom-up approach. The
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17 91 methodology is consistent with previously published research in this field in Australia
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20 92 and internationally.[14-16] Costs were estimated from the perspective of Australian
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23 93 society for the 2016-17 financial year.

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25 94 In this study, the financial costs of delirium to the Australian health system include
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27 95 the costs of running hospitals and nursing homes, general practitioner (GP) and
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29 96 specialist services reimbursed through Australia's universal health insurance scheme
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31 97 and private funds, the cost of pharmaceuticals and over-the-counter medications,
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33 98 allied health services, research and health administration. The other financial costs
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35 99 of delirium in this study include productivity costs, informal care, funeral costs, and
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37 100 deadweight losses associated with taxation payments and administration. The loss of
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39 101 wellbeing due to delirium was measured using disability adjusted life years (DALYs).

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41 102 A targeted literature review was conducted to identify the prevalence of delirium in
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43 103 acute hospitalizations, nursing homes and in the community (without presenting to
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45 104 hospital). The review also covered costs, productivity and other outcomes (e.g.
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47 105 mortality and burden of disease) due to delirium. The targeted review was
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49 106 investigative in nature and considered fit-for-purpose as the prevalence and
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3 107 methods vary widely across studies. Searches were conducted using PubMed in June
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5 108 2017.

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9 109 Studies were included if they were conducted in a hospital setting, and covered
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11 110 general hospital wards (medical or surgical) reflective of an acute setting. Studies
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13 111 were also included if they included costs of delirium, including health system,
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15 112 productivity, carer and wellbeing costs. Studies were excluded from the analysis if
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17 113 they did not measure prevalence using validated diagnostic measures, or if they did
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19 114 not report on costs or outcomes from delirium. Studies were further excluded if they
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21 115 did not report on primary or administrative data. No specific date restrictions were
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23 116 applied to the literature review due to the investigative nature of it. The specific
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25 117 search terms used in the literature review are available in Additional File 1.

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28 118 Results from the literature searches were generally pooled by taking a weighted
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30 119 average of outcomes or results. Additional grey literature (e.g. government statistics)
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32 120 were also collated and these documents provide many of the necessary inputs for
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34 121 this cost of illness study.

35 36 37 38 39 40 41 122 **Prevalence**

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45 123 The prevalence of delirium in Australian hospitals was estimated by taking a
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47 124 weighted average across identified studies (see Additional File 1, Table 1).

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49 125 Prevalence was then applied to overnight acute emergency hospital separations for
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51 126 people aged 70 years or older in 2016-17 to estimate separations due to delirium in
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53 127 elderly people in that year.[17]
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3 128 Additional diagnosis separations in younger age groups (less than 70 years old) were
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5 129 estimated by applying the ratio between total and principal delirium diagnoses to
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8 130 principal diagnoses in the younger age groups. [17,18]
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11 131 No prevalence studies in Australian nursing homes were identified. Prevalence
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13 132 results were thus derived from a study from the Netherlands,[19] due to similarities
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15 133 in aged care settings, demographic profiles and medication prescribing rates – for
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17 134 example, both countries exhibit high rates of psychotropic medication prescribing
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19 135 (though there are some differences in the preferred antipsychotic agent),[20]
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21 136 despite their limited efficacy and adverse effects in people with delirium.[7] The
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23 137 combined prevalence and incidence was 8.5% and 16.9 per 100 person-years
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25 138 respectively. These rates are similar to the rates reported in other international
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27 139 literature.[21-23] These rates were applied to the number of permanent residents in
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29 140 aged care facilities in Australia, adjusting for population growth by age group from
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31 141 the Australian Bureau of Statistics (ABS).[24]
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39 142 The total prevalence of delirium in Australia 2016-17 was adjusted to avoid double
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41 143 counting people in the residential aged care cohort who also present to hospital. The
42
43 144 following rates were used to adjust the prevalence to avoid double counting people
44
45 145 in residential aged care who also present to hospital: 50% of cases were delirious at
46
47 146 admission;[25] 43% of hospitalized patients with delirium during their stay were
48
49 147 delirious at discharge (5.5% delirious at discharge, 12.7% with delirium);[26] 31.2%
50
51 148 were admitted from residential aged care while 68.9% were admitted from the
52
53 149 community;[27] and of people with delirium, 28% of patients were discharged to
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3 150 residential aged care, 63% were discharged to the community, and 9% died before
4
5
6 151 discharge from hospital.[28]
7

8 9 152 **Average duration of an episode of delirium and mortality**

10
11
12 153 The average duration of delirium was estimated by taking a weighted average of the
13
14 154 findings reported in twelve studies (Additional File 1, Table 2).
15

16
17 155 Mortality associated with delirium was estimated using an attributable fraction
18
19
20 156 approach,[13] and a hazard ratio of 1.77 that was based on a previous systematic
21
22 157 review and meta-analysis (Additional File 1, Table 3).[3]. The hazard ratio was used
23
24
25 158 to estimate an attributable fraction for how many deaths are due to delirium in
26
27 159 Australia.
28

29 30 160 **Health care system expenditure**

31
32
33 161 Health system costs were estimated using a bottom-up approach. This includes costs
34
35
36 162 associated with hospital, medication, and research expenditure, out of hospital
37
38 163 medical and other health professionals' expenditure, and residential aged care
39
40
41 164 expenditure. Delirium induces functional decline, resulting in a longer length of stay
42
43 165 (LOS) for older people in hospital, consequently leading to higher hospitalization
44
45 166 expenditure.[2] To estimate the additional expenditure, the prevalence of delirium
46
47
48 167 among hospitalized older people was applied to the additional LOS and the average
49
50
51 168 daily cost of care in a hospital setting.
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53
54 169 The average daily cost of an acute separation was obtained from the Independent
55
56 170 Hospital Pricing Authority (IHPA) for 2014-15 and adjusted by the standard index
57
58 171 rate used by IHPA (2.1%) to estimate the cost for the 2016-17 base year.[29] The
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3 172 average daily cost was also adjusted by an additional 14.3% to inflate for non-
4
5
6 173 allocated health costs (an allowance for capital costs) based on AIHW.[30]
7
8
9 174 Delirium can also be recorded as an additional diagnosis in Australian hospital data,
10
11 175 where delirium contributes to a greater length of stay in hospital. The cost
12
13 176 associated with an increased length of stay was estimated using the average daily
14
15 177 cost of any hospital separation, which was further adjusted to remove separation
16
17 178 costs that are unlikely to be attributable to delirium, such as costs associated with
18
19 179 surgery. Where delirium was a primary diagnosis, the cost was assumed to be the
20
21 180 same as the delirium diagnostic resource group, which was £4,489 in 2016-17 after
22
23 181 updating for inflation in the National Efficient Price.[29]
24
25
26
27
28
29 182 Health research expenditure on delirium in Australia in 2016-17 was estimated using
30
31 183 data from the National Health and Medical Research Council (NHMRC) grants
32
33 184 database. The database outlines all NHMRC research grant funding between 2000
34
35 185 and 2016 and provides a description of the projects and key outcomes achieved.[31]
36
37
38 186 Annual funding allocated to delirium research in 2016-17 was estimated by taking an
39
40 187 average across the historical years. Other forms of health research where research
41
42 188 costs can be recovered – for example, by charging a higher price for services – were
43
44 189 not considered in this analysis, consistent with standard methodology.[13]
45
46
47
48
49 190 Out of hospital medical expenditure (GP consultations) was estimated by applying
50
51 191 the average cost per GP consultation (approximately £16 after adjusting for multiple
52
53 192 problems per GP consultation) to the total services associated with organic
54
55 193 psychoses in Australia,[32, 33] which was considered comparable to delirium.
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3 194 Residential aged care expenditure was estimated using an attributable fraction
4
5 195 approach based on literature to estimate admissions to aged care due to cognitive
6
7
8 196 decline associated with delirium. The odds ratio for admission (2.41),[4] was
9
10 197 converted to an attributable fraction. The number of admissions was adjusted by
11
12 198 average LOS in residential aged care in Australia and applied to the average costs
13
14 199 associated with residential aged care, which is approximately £43,978 per person in
15
16 200 aged care.[34]

21 **Other financial costs**

22
23
24 202 The economic cost of short run productivity losses associated with absenteeism
25
26 203 were estimated using the friction cost method.[13] The absenteeism cost due to
27
28 204 delirium was estimated by multiplying the average duration of delirium by the
29
30 205 number of hospital separations that occur in the working age population, adjusted
31
32 206 for general population employment rates. Average employment rates and average
33
34 207 weekly earnings for people with delirium are based on ABS data for the general
35
36 208 population by age and gender.[35, 36]

37
38
39 209 Carers are people who provide care to others in need of assistance or support. An
40
41 210 informal carer provides this service without formal payment and does so outside of
42
43 211 the formal care sector. Evidence suggests that people with delirium experience a
44
45 212 decline in functioning, such that they are unable to perform as many usual activities
46
47 213 of daily living following delirium.[37, 38] Estimates of the hours of informal care
48
49 214 provided to people with delirium was based on this expected decline in activities of
50
51 215 daily living. The dollar value of informal care was estimated as the opportunity cost
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3 216 of a carer's time, which was based on general population average weekly earnings
4
5
6 217 and employment rates.[35, 36]
7

8
9 218 The additional cost of funerals borne by family and friends of people with delirium
10
11 219 was based on the number of deaths associated with delirium. The cost of a funeral
12
13 220 was assumed to be £4,602. Funeral costs were brought forward by the average life
14
15 221 expectancy at age of death. The deadweight losses due to lost taxation revenue
16
17 222 (given an assumption of no change in spending) and additional government spending
18
19 223 on delirium was calculated by applying the average marginal excess burden of
20
21 224 taxation of £0.31 per £1 of tax.[39, 40]
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25

26 225 **Loss of wellbeing**

27
28
29 226 Burden of disease methodology was employed to quantify the impact of delirium on
30
31 227 wellbeing.[41] The approach is non-financial, where pain, suffering and premature
32
33 228 mortality are measured in terms of disability adjusted life years (DALYs). DALYs are
34
35 229 comprised of years of healthy life lost due to morbidity (YLDs) and years of life lost
36
37 230 due to premature mortality (YLLs).[41] YLDs were calculated using a prevalence
38
39 231 approach, whereby the disability weight was multiplied by average duration of
40
41 232 delirium. The disability weight for delirium used in this study was 0.17.[42] Duration
42
43 233 of delirium was based on the prevalence of persistent delirium over 12 months.[43]
44
45 234 DALYs were converted to a monetary value using the value of a statistical life year
46
47 235 (£93,882), which is an official estimate updated for inflation using the Consumer
48
49 236 Price Index.[44] The value of a statistical life year was discounted at a rate of 3% per
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3 237 annum,[13] where it was applied to future years of life lost due to mortality from
4
5
6 238 delirium.

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8
9 239 **Costs of dementia attributable to delirium**

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11 240 Costs of dementia were sourced from an Australian cost of illness study.[45] Inputs
12
13
14 241 were taken for Australia in the 2016 financial year, and updated using either health
15
16
17 242 inflation or the Consumer Price Index as appropriate. The wellbeing cost attributable
18
19 243 to dementia for YLLs or YLDs was estimated using data from the Australian Institute
20
21 244 of Health and Welfare's Australian Burden of Disease Study.[46] The proportion of
22
23
24 245 dementia attributable to delirium was estimated using the population attributable
25
26
27 246 fraction approach. The odds ratio for developing a new case was 5.88 for people
28
29 247 aged 65-84 years old and 7.56 for people aged 85 years or older,[47-49] which was
30
31 248 used to estimate the attributable fraction.

32
33
34 249 **Sensitivity analysis**

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36
37 250 One-way sensitivity analyses were conducted on prevalence, the risk for mortality,
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39 251 dementia admission to aged care, average hospital costs, discount rate for DALYs,
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41
42 252 and the value of a statistical life year. The specific values represent the upper and
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44
45 253 lower 95% confidence intervals for the relevant input parameters where available, or
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47 254 unit costs that were 25% higher or lower if the distribution was unknown.

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49
50 255 **Currency standardization**

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53 256 All costs are expressed in 2016-17 pound sterling. Costs were converted from
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55
56 257 Australian dollars using the 2017 Organisation for Economic Cooperation and
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3 258 Development purchasing power parity of 2.065 Australian dollars per pound sterling
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6 259 in 2017.[50]
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8 9 260 **Data analysis and ethical considerations**

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11 261 Data for this study was collected throughout January to June 2017 by the authors
12
13
14 262 from a range of public data sources and literature. The data was analyzed and
15
16
17 263 compiled in Microsoft Excel. No individual patient data was collected for the study
18
19 264 and therefore, this study did not require ethics approval.
20
21

22 265 **Patient and public involvement**

23
24
25 266 Patient and public were not involved in the design or planning of this study.
26
27

28 29 267 **RESULTS**

30 31 32 268 **Prevalence and mortality**

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34
35 269 Overall, the prevalence of delirium in a hospital setting was estimated to be 20.2%
36
37 270 on average, which was applied to the 521,099 overnight acute emergency hospital
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39 271 separations for people aged 70 years or older in 2016-17. Therefore, there were an
40
41 272 estimated 105,182 hospital separations involving delirium in 2016-17, of which
42
43 273 delirium was recorded as the principal diagnosis for approximately 11,999
44
45 274 separations in 2016-17. In addition, there were an estimated 14,578 separations for
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47 275 younger Australians, and 119,760 total cases of delirium in Australian hospitals in
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49 276 2016-17.
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55 277 In Australia on 30 June 2015, there were 172,044 permanent residents in aged care
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57 278 facilities. There were an estimated 181,314 permanent residents in Australian aged
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60

279 care facilities on 30 June 2017 after adjusting for population growth by age group.

280 Applying the prevalence (at baseline), and the incidence per 100 person years from

281 Boorsma et al,[19] it was estimated that 46,054 permanent residents had at least

282 one episode of delirium in 2016-17.

283 After adjusting for the interactions between delirium in aged care and hospital

284 settings, there were an estimated 132,595 cases of delirium in Australia in 2016-17,

285 representing cases that occur in both settings. This is equivalent to approximately

286 0.5% of the population in Australia, although some individuals may experience

287 delirium more than once in a year. Prevalence by age and gender are available in

288 Table 1. The rates increase substantially with age.

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

<i>Age/ gender</i>	<i>Community</i>	<i>Residential aged care</i>	<i>Total</i>	<i>% of general population</i>
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
<i>Total</i>	<i>44,149</i>	<i>14,801</i>	<i>58,949</i>	<i>0.5</i>
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
<i>Total</i>	<i>42,393</i>	<i>31,253</i>	<i>73,646</i>	<i>0.6</i>
Person	86,541	46,054	132,595	0.5

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3 291 The hazard ratio for mortality indicated that 12,571 people who had delirium would
4
5 292 die, and an estimated 909 deaths were attributable to delirium itself in 2016-17.
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8 293 **Health care system expenditure**

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10
11 294 Delirium most commonly occurred in hospitals in Australia in 2016-17, with an
12
13 295 estimated 119,760 cases (some of these individuals usually reside in aged care).
14
15
16 296 Delirium was recorded as the primary diagnosis in 13,662 separations at an average
17
18 297 cost of £4,489 per separation in 2016-17. Delirium was recorded as an additional
19
20 298 diagnosis in a further 106,098 separations. The average daily cost for an additional
21
22 299 separation was estimated to be £644, which was multiplied by the number of cases
23
24 300 and the additional LOS due to delirium, which was estimated to be 2.7 days (see
25
26 301 Additional File 1, Table 4 and Additional File 1, Table 5). After adjusting for
27
28 302 population growth, there were estimated to be 22,640 GP consultations associated
29
30 303 with delirium in 2016-17, which was multiplied by £16 per consultation to estimate
31
32 304 total GP costs.
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39 305 Total health system and aged care costs associated with delirium in Australia were
40
41 306 estimated to be £844.2 million in 2016-17. The total comprised hospital
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43 307 (£247.3 million), residential aged care (£596.2 million), out-of-hospital medical (£0.4
44
45 308 million), and research expenditure (£0.3 million).
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49 309 **Other financial costs**

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51
52 310 On average, it was estimated that each person with delirium received an additional
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54 311 0.9 hours of care per week, based on the change in activities of daily living over a
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56 312 period of 12 months (Additional File 1 provides supplementary information that was
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1
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3 313 used to estimate the additional hours of care). Thus, informal carers provided an
4
5 314 estimated 987,958 hours of care in 2016-17, which was valued at £0.8 million. The
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7
8 315 cost of informal care (£0.8 million) is relatively small due to the low opportunity cost
9
10 316 of carer time (£0.84 per hour).

11
12
13 317 We estimate that working age people with delirium were absent from work for
14
15
16 318 44,590 days in 2016-17, which was valued at £6.6 million using average weekly
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18 319 earnings for the general population.

20
21 320 Finally, brought forward funeral costs were estimated to be £0.7 million and
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23
24 321 deadweight losses were estimated to be £188.4 million in Australia 2016-17. Thus,
25
26 322 total other financial costs (informal care, absenteeism, brought forward funeral costs
27
28 323 and deadweight losses) were estimated to be £196.6 million in Australia in 2016-17.
29
30 324 Productivity losses imposed by delirium were estimated to be relatively small as
31
32 325 delirium largely occurs in the elderly population.

33 34 35 36 37 326 **Loss of wellbeing**

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39
40 327 The total burden of disease from delirium in 2016-17 was estimated to be
41
42 328 £994.1 million. Overall, delirium resulted in an estimated: 5,441 years of healthy life
43
44 329 lost due to disability (YLDs), or 0.041 YLDs per person with delirium; 5,687 years of
45
46 330 life lost due to premature death (YLLs), or 0.043 YLLs per person with delirium; and
47
48 331 11,128 DALYs overall, or around 0.084 DALYs per person with delirium in 2016-17.

50 51 52 53 332 **Costs of dementia attributable to delirium**

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55
56 333 Overall, it was estimated that 40,981 or 10.6% cases of dementia were attributable
57
58 334 to delirium, which largely occur in people aged 85 years or older. The total costs of

335 dementia due to delirium were estimated to be £2.2 billion in Australia in 2016-17,
 336 of which the financial costs were £675.7 million and the loss of wellbeing was
 337 £1.6 billion. Table 2 shows cost breakdowns by age and gender group. Figure 1
 338 shows the costs of dementia due to delirium broken down by health system and
 339 aged care costs, other financial costs and burden of disease.

340 Table 2. Estimated costs of delirium in Australia in 2016-17, by age and gender group,
 341 £ million or %

<i>Age/ gender</i>	<i>Financial cost</i>		<i>Wellbeing cost</i>		<i>Total</i>	<i>% of total</i>
	<i>Delirium</i>	<i>Dementia due to delirium</i>	<i>Delirium</i>	<i>Dementia due to delirium</i>		
Male						
<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	

342

343 (INSERT FIGURE 1)

344 **Total costs**

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

18

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

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

<i>Cost component</i>	<i>Total (£ million)</i>	<i>Per person with delirium (£)</i>
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

352 Sensitivity analysis

353 The results and specific values for the sensitivity analysis are shown in Table 4 and
 354 Figure 2. The total cost of delirium in Australia was most sensitive to changes in the
 355 risk for dementia following delirium and the overall prevalence rate. The total cost of
 356 delirium was estimated to range from £2.6 billion to £5.9 billion in Australia in
 357 2016-17.

358 Table 4. Sensitivity analysis, £ million

<i>Variable</i>	<i>Financial</i>	<i>Loss of wellbeing</i>	<i>Total</i>
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

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

360

361 (INSERT FIGURE 2)

362 DISCUSSION

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

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3 368 is critical that such economic estimations are undertaken as they inform decision
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6 369 making.

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9 370 According to these estimates, delirium imposes a substantial burden on society.

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11 371 Considering delirium alone, the economic costs were mostly incurred by the health
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13 372 and aged care systems (£844.2 million), representing close to 1.5% of total
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16 373 expenditure on health and aged care in Australia. As many high-income western
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18 374 countries are dealing with issues of aging demographics and cognitive impairment,
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20 375 the findings may be generalizable to other health and aged care systems. For
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22 376 example, previous research has found that delirium is associated with multiple
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24 377 adverse outcomes including increased length and cost of hospitalization, functional
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26 378 and cognitive decline, institutionalization, and mortality.[2-5, 51] These results have
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28 379 significant implications for governments, who aim to identify conditions with high
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30 380 social and financial costs for focused attention through public education and other
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32 381 initiatives that effect improvements in health status. The results of this study
33
34 382 highlight the need for concerted, worldwide efforts to mitigate the impacts of this
35
36 383 clinically significant and costly medical condition.

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39 384 According to these estimates, there were 132,595 occurrences of delirium in
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41 385 Australia in 2016-17, but data from the Australian Institute of Health and Welfare
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43 386 National Hospital Morbidity Database for 2015-16 indicate that as many as 1 in 5
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45 387 cases are missed. This is supported by previous research which suggests that
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47 388 delirium is undiagnosed in a large number of cases, ranging from approximately 25%
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49 389 of cases up to 87.5% in cases where dementia is also present.[12] This has significant
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3 390 implications for clinical practice as the outcomes of delirium are serious.[1] Future
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5 391 research could focus on techniques to improve the detection rate.
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9 392 Dementia represents a significant cost to the economy of all countries; the cost of
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11 393 dementia due to delirium is therefore an important cost component of delirium. It
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13 394 has been estimated that 47 million people are living with dementia globally, with
14
15 395 costs of £583 billion in 2015 (original estimate converted from US dollars to pound
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17 396 sterling using purchasing power parity of 0.713);[50, 52] moreover, prevalence is
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19 397 expected to triple over the next three decades.[52] Overall, the costs of dementia
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21 398 attributable to delirium more than doubled the total costs of delirium in Australia in
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23 399 2016-17. It was estimated that approximately 10.6% of dementia cases, and thus
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25 400 costs, are associated with delirium. Therefore, delirium imposes a large cost burden
26
27 401 on residential aged care, due to the high prevalence of dementia and the strong
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29 402 relationships between cognitive impairment and aged care. There may be
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31 403 considerable opportunities to prevent some of the worldwide burden of dementia
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33 404 and improve the fiscal sustainability of health systems in the face of aging
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35 405 populations.
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43 406 Care for delirium following discharge from hospital relies heavily on informal carers,
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45 407 who provided almost 1 million hours of care to people with delirium. As workforce
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47 408 participation increases and the propensity to care declines,[53] there is a risk that
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49 409 the care needs of people with delirium will either go unmet, or require additional
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51 410 government funding for aged care to meet their needs.
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3 411 There are some limitations to this study. First, the methods outlined the use of a
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5 412 non-systematic search strategy, noting that this was fit-for-purpose when a number
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8 413 of inputs were derived from official Australian Government statistics. The estimates
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10 414 presented should be interpreted with this in mind. Second, limited studies were
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13 415 found with appropriate methods to robustly estimate the prevalence of delirium in
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15 416 Australian hospital settings, but also in community or residential aged care settings.
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18 417 In order to minimize the impact of this limitation and the risk of double counting
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20 418 across studies, the analysis focused on delirium which met the full diagnostic criteria.
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23 419 Similarly, data paucity in some areas, such as out-of-hospital medical costs and
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25 420 productivity losses (employment outcomes) means that total estimates may be
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27 421 conservative. Given the methodology, the costs of delirium presented in this paper
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29 422 should be treated as an estimate only. More research, including observational
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31 423 studies in Australian settings, is required to understand the true costs incurred by
32
33 424 people with delirium. However, a study that can capture costs across the health
34
35 425 system and aged care settings in Australia will be technically challenging and may
36
37 426 not be feasible due to the fragmented nature of the systems and data collection –
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39 427 particularly beyond the point at which people interact with the system. Finally, cost
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41 428 of illness studies provide guidance on the size of the problem, but are only useful for
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43 429 informing cost effective options for change when compared to the cost of such
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45 430 interventions. More work is needed to identify cost effective options to reduce the
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47 431 burden of delirium in Australia.
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55 432 **CONCLUSION**

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3 433 In summary, delirium imposes a substantial burden on Australian society – both in
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6 434 terms of financial costs associated with health system expenditure and a greater
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8 435 need for residential aged care due to the functional and cognitive decline associated
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11 436 with delirium and dementia. The financial costs of delirium were largely borne by
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13 437 Australian governments due to the health system and aged care expenditure.

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16 438 Further research should seek to understand the causes, treatment and prognosis of
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18 439 delirium, especially with regard to potential pathways from an episode of delirium to
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21 440 subsequent mortality outcomes and reduced cognitive functioning. Improving
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23 441 mortality outcomes and reducing decline in cognitive functioning would help to
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25
26 442 reduce the substantial financial and wellbeing costs of delirium.

27 28 29 443 **ACKNOWLEDGEMENTS**

30 31 32 444 **Author contributions:**

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35 445 LP, JS and GC conceived of and designed the study. JS, JH and LP collated the data,
36
37 446 performed the data analysis and contributed to interpretation and reporting of the
38
39 447 data. AT, MA and GC contributed to the interpretation and reporting of the data. All
40
41 448 authors read, commented on and approved the final manuscript, and all authors
42
43 449 reviewed the manuscript for important intellectual content. The sponsor was not
44
45 450 directly involved in the findings of the research.

46 47 48 451 **Conflicts of interest**

49
50
51 452 The authors declare that they have no competing interests.

52 53 54 453 **Funding sources**

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3 454 The research was supported by the Australasian Delirium Association.
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6 455 **Data sharing statement**
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9 456 No additional data are available.
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12 457 **FIGURE LEGENDS**
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16 458 Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £
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18 459 million.

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21 460 Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter
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23 461 inputs on the total cost of delirium in Australia in 2016 17.
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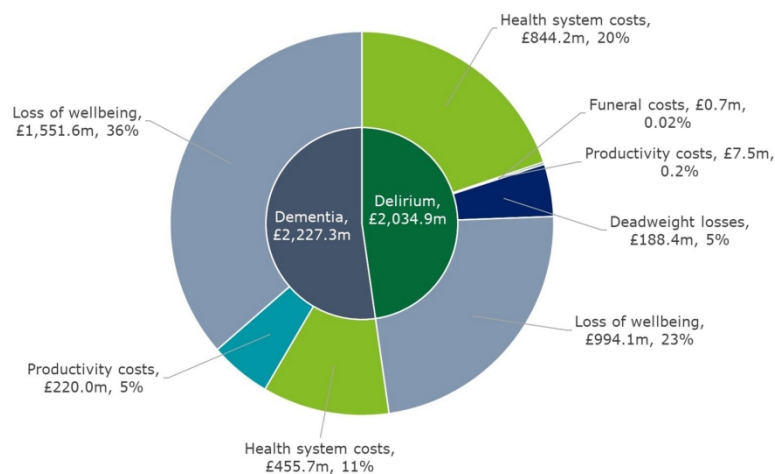


Figure 1 Costs of delirium and dementia due to delirium in Australia in 2016-17, £ million

174x90mm (300 x 300 DPI)

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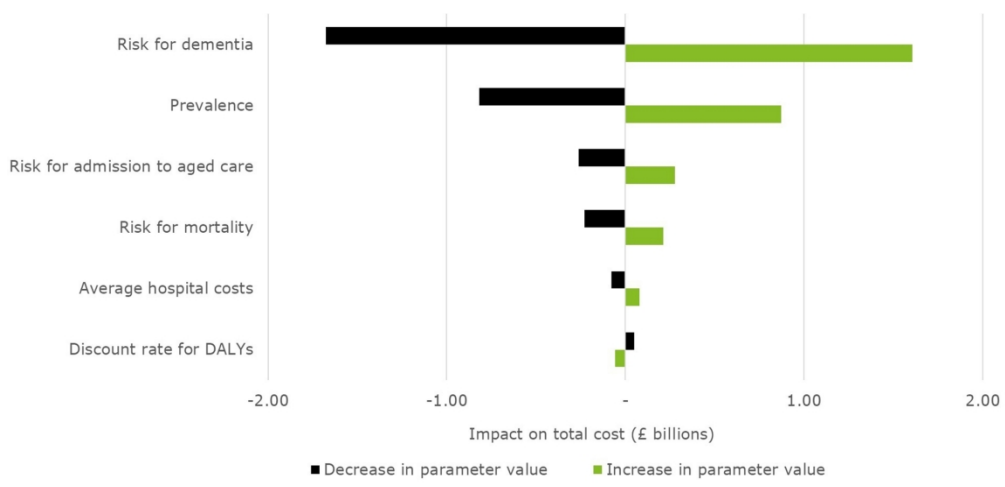


Figure 2 Sensitivity analysis (tornado diagram) showing the impact of key parameter inputs on the total cost of delirium in Australia in 2016-17

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

1	1	CHEERS checklist	2
2	2	Literature review strategy	4
3	3	Epidemiology	5
4	3.1	Prevalence in episodes of acute hospital care	5
5	3.2	Duration of delirium episodes.....	6
6	3.3	Mortality associated with delirium	7
7	4	Hospital expenditure	9
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For peer review only

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

10 1 CHEERS checklist

11 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	<i>Single study-based estimates:</i> 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	<i>Synthesis-based estimates:</i> 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	<i>Single study-based economic evaluation:</i> 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	<i>Model-based economic evaluation:</i> 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.

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

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	<i>Single study-based economic evaluation:</i> 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	<i>Model-based economic evaluation:</i> 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.

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

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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34 **3 Epidemiology**

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

38 **3.1 Prevalence in episodes of acute hospital care**

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

42 **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 al⁴						
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 al⁴ 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
Iseki 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 al⁴ 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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49 **3.3 Mortality associated with delirium**

50 Delirium is associated with higher rates of mortality in hospital settings, and a greater chance of
 51 mortality occurring in the year following an episode of delirium. Mortality was estimated using an
 52 attributable fraction approach based on literature. Witlox et al³¹ reported an overall average
 53 mortality rate of 38.0% compared to a rate of 27.5% with no delirium, which was a 1.4-fold increase
 54 for those with delirium. The hazard ratio – indicating how much more likely someone with delirium
 55 is to have died at any point in time – was estimated to be 1.95. The authors included seven studies
 56 from the US, UK, Canada, Chile and Brazil. To estimate mortality associated with delirium for
 57 Australia, the Chilean and Brazilian studies have been excluded from the analysis as they are
 58 demographically less similar to Australia and there may be alternative drivers of mortality in those
 59 countries. The hazard ratio was re-estimated by meta-analysis using a random effects model. The
 60 final reweighted hazard ratio was estimated to be 1.77 (Table 3).

61 **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)

62 **Source:** Based on Witlox et al³¹

63 The hazard ratio (1.77) based on data from Witlox et al³¹ was applied to general population mortality
 64 rates, including the 1.4-fold increase for mortality for people who had delirium, for the respective
 65 age groups to estimate the number of deaths associated with delirium in 2016-17. It was expected
 66 that 12,571 people who had delirium would die in 2016-17, noting not all mortality is due to delirium
 67 itself (e.g. comorbid dementia or other illness may contribute to both delirium and death). Deaths

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3 68 due to delirium were estimated by applying the population attributable fraction to total deaths in
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5 69 the delirium cohort in 2016-17.^b
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^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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70 **4 Hospital expenditure**

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

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

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

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84 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

85 Source: as itemised in table.

86 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

87 Source: as itemised in table.

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88 **5 Informal care costs**

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

93 Bellelli et al⁵⁵ found that 26.2% of patients who developed delirium during their hospital stay
94 required assistance from paid caregivers following discharge. The rate of paid caregiving was
95 assumed to be comparable to informal care in Australia as the care is usually provided by family
96 members. In order to estimate the number of care recipients for Australia, 26.2% was applied to the
97 prevalence of delirium for people who are 65 years or older and who live in the community (total
98 adjusted prevalence – prevalence in aged care). Therefore, it was estimated that 20,741 people
99 would require care due to delirium in Australia in 2016-17. People with delirium required assistance
100 with an additional 0.36 activities of daily living over a period of 12 months.^{56,57}

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

105 The carer's opportunity cost of time was calculated based on the weighted average weekly
106 earnings⁵⁴ 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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