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Is length of time in a stroke unit associated with better outcomes for patients with stroke in Australia? An observational study

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27 **Abstract**

28 **Objective:** Spending at least 90% of hospital admission in a stroke unit (SU) is a
29 recommended indicator of receiving high quality stroke care. However, whether this makes a
30 difference to patient outcomes is unknown. We aimed to investigate outcomes and factors
31 associated with patients with acute stroke spending at least 90% of their admission in a SU,
32 compared to those having less time in the SU.

33 **Design:** Observational study using cross-sectional data

34 **Setting:** Data from hospitals who participated in the 2015 Stroke Foundation National Audit:
35 Acute Services (Australia) and had a SU. This audit includes an organizational survey and
36 retrospective medical record audit of approximately 40 admissions from each hospital.

37 **Participants:** Patients admitted to a SU during their acute admission were included.

38 **Outcome measures:** Hospital-based patient outcomes included length of stay, independence
39 on discharge, severe complications and discharge destination. Patient, organizational, and
40 process indicators were included in multilevel logistic modelling to determine factors
41 associated with spending at least 90% of their admission in a SU.

42 **Results:** Eighty-eight hospitals with a SU audited 2655 cases (median age 76 years, 55%
43 male). Patients who spent at least 90% of their admission in a SU experienced: a length of
44 stay that was two days shorter (coefficient -2.77 95% CI -3.45, -2.10), fewer severe
45 complications (aOR: 0.60; 95% CI: 0.43, 0.84) and were less often discharged to residential
46 aged care (aOR: 0.59; 95% CI: 0.38, 0.94) than those who had less time in the SU. Patients
47 admitted to a SU within three hours of hospital arrival were three times more likely to spend
48 at least 90% of their admission in a SU.

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3 49 **Conclusion:** Spending at least 90% of time in a SU is an excellent measure of stroke care
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5 50 quality as it results in improved patient outcomes. Direct admission to stroke units is
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7 51 warranted.
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11 12 13 53 **ARTICLE SUMMARY**

14 15 16 54 **Strengths and limitations of this study:**

- 17
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19 55 • While spending 90% of time in the SU is considered an important quality of care measure,
20
21 56 there is limited evidence that this is associated with better outcomes in patients with stroke. A
22
23 57 strength of this research is that it has provided further evidence of the importance which has
24
25 58 implications for clinical practice and development of new models of stroke care.
- 26
27
28 59 • The study involved a large comprehensive dataset, which provided national representation.
- 29
30
31 60 • Standardised data collection and an inclusive data dictionary was provided to data
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33 61 abstractors to minimise reporting bias and ensure data were reliably collected.
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36 62 • For some outcomes, only dates, rather than times were collected, which would have
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38 63 provided more accuracy

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70 **Introduction**

71 Stroke remains a major global health challenge because it is a leading cause of death
72 and major disability.¹ It is well-established that patients treated in stroke units (SUs) are more
73 likely to receive evidence-based clinical practices, have better survival and self-rated quality
74 of life compared to those receiving care in other wards.²⁻⁴ It is recommended that people with
75 stroke should be admitted directly to a SU, preferably within three hours of stroke onset,⁵ and
76 that they should also be treated in a SU throughout their admission unless their stroke is not
77 the main clinical problem.⁶ Therefore, spending most (at least 90%) of hospital admission in
78 a SU is recommended as one of the important indicators of high quality acute stroke care.^{7,8}

79 However, there is limited evidence that this process of care is associated with better
80 outcomes in patients with stroke. We aimed to investigate outcomes and factors associated
81 with patients with acute stroke spending at least 90% of their admission in a SU, compared to
82 those having less time in the SU.

83 **Materials and methods**

84 The description and reporting of this study is based on the Strengthening the
85 Reporting of Observational Studies in Epidemiology (STROBE) statement.⁹

86 **Study design and data source**

87 This observational study used data from hospitals participating in the Australian
88 Stroke Foundation Acute Services Audit Program conducted in 2015. The audit program is
89 run biennially to provide cross-sectional data on clinical performance, and has two
90 components: an organizational survey and clinical audit.¹⁰ Detailed methods for the Audit
91 Program have been described elsewhere.¹⁰ In brief, data obtained in the organizational survey
92 are used to describe aspects of acute stroke services, including bed numbers, admissions per
93 year and available resources e.g. stroke units. Data collected in the clinical audit are used to

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3 94 identify adherence to clinical guidelines and provide evidence on areas to improve the quality
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5 95 of care. Participation in the audit was voluntary and all Australian acute stroke services
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7 96 admitting at least three acute stroke patients per year were eligible to participate. Data for the
8
9 97 first 40 or more consecutive acute stroke admissions (from 1 September 2014 and discharged
10
11 98 by 28 February 2015) were collected by trained data abstractors from June to August 2015.
12
13 99 To obtain a more representative sample, larger hospitals were encouraged to provide more
14
15 100 cases. Patients with a primary diagnosis of acute stroke (ICD-10 codes: I61, I62.9, I63, I64)
16
17 101 were eligible to be included in the audit.
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19

102 **Patient population and definitions**

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23 103 Data for patients who were treated at a hospital with a SU and only those patients
24
25 104 admitted to a SU during their acute admission were included. Time spent in a SU (SU time)
26
27 105 was determined by subtracting the date of discharge from the SU, from the date of admission
28
29 106 to the SU. To determine patients who spent at least 90% of their admission in a SU, the SU
30
31 107 time was divided by total length of stay (LOS) in the hospital (total LOS; calculated by
32
33 108 subtracting date of discharge from hospital or death from date of admission to hospital) and
34
35 109 the result multiplied by one hundred ($[\text{SU time}/\text{total LOS}] * 100$). We further determined
36
37 110 early/late admission to the SU as ≤ 3 hours versus > 3 hours from arrival to the emergency
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39 111 department (ED) to admission on the SU. For patients whose stroke occurred while they were
40
41 112 already in hospital, date of stroke onset was used as a surrogate for date of admission to
42
43 113 hospital and arrival to ED.
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47 114 The following patient outcomes were assessed: LOS, death, level of independence on
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49 115 discharge, severe complications and discharge destination. LOS was defined as the total
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51 116 length of time from admission to the hospital to discharge from the hospital or death. Level of
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53 117 independence on discharge was defined as a modified Rankin scale (mRS) score of zero to
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55 118 two. A severe complication was a new event in hospital considered to be incapacitating, life
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3 119 threatening and one that prolonged hospital admission such as pneumonia, falls, fever,
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5 120 urinary tract infection, seizures and deep vein thrombosis. Discharge destinations included
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7 121 private residence, inpatient rehabilitation or residential aged care facility.

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9 122 Only valid yes/no responses were included in the analyses for data related to medical
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11 123 history and the presence of symptoms on presentation to hospital. For data relating to
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13 124 processes of care, e.g. received care in a SU, not documented and unknown responses were
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15 125 assumed to be negative and included in the denominator. To minimise bias, only patients with
16
17 126 valid admission and discharge (SU and hospital) time or date were included.

127 **Statistical analysis**

128 Univariable analyses were performed to determine differences between patients who
129 spent at least 90% and those who spent less than 90% of their admission in a SU. The chi-
130 square test was used for categorical variables. The nonparametric Wilcoxon Mann-Whitney
131 rank sum test was used for continuous variables that were not normally distributed.

132 Multilevel random effects logistic regression analyses, with level defined as hospital
133 were undertaken to determine:

- 134 i) the association between spending at least 90% of admission in a SU and in-
135 hospital outcomes such as death, level of independence on discharge (mRS 0-2),
136 severe complications and various discharge destinations.
- 137 ii) factors associated with spending at least 90% of the admission in a SU.

138 For the continuous outcome of LOS, a median regression model with bootstrap
139 estimated standard errors was undertaken. A parsimonious approach to multivariable model
140 development was used and independent variables with statistical significance ($p \leq 0.05$) from
141 univariable analyses were included.

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3 142 To determine factors associated with spending at least 90% of the admission in a SU,
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5 143 independent variables considered for inclusion in multivariable analyses were patient factors
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7 144 e.g. age; health system factors e.g. private hospital, presence of a stroke care coordinator and
8
9 145 onsite neurosurgery; and clinical process factors e.g. admission to SU within three hours of
10
11 146 arrival to ED. Other potential confounders including stroke type (ischemic vs intracerebral
12
13 147 hemorrhage and unknown) and stroke severity factors such as inability to walk, arm
14
15 148 weakness, and speech impairment on admission and incontinence within 72 hours, which are
16
17 149 based on the Counsell et al validated prognostic model for comparing patient outcomes,¹¹
18
19 150 were included. This validated model¹¹ has been compared against a model using age plus
20
21 151 scores on the National Institutes of Health Stroke Scale and both prognostic models
22
23 152 performed well overall, thus the choice between them should be based on clinical and
24
25 153 practical considerations.¹²
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29 154 Models for association between length of time spent in a SU and in-hospital outcomes
30
31 155 were adjusted for patient characteristics (e.g. premorbid function and past history of atrial
32
33 156 fibrillation), variables with clinical importance (e.g. sex and age), stroke type and stroke
34
35 157 severity factors. Sensitivity analyses, including other cut offs for percentage of admission
36
37 158 spent in a SU (e.g. ≥ 50 to <60 , ≥ 60 to <70 , ≥ 70 to <80 , ≥ 80 to <90) were undertaken to
38
39 159 determine a potential dose effect with LOS, severe complications, and independence on
40
41 160 discharge.
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44 161 Standard techniques were implemented to check for collinearity. Values of $p < 0.05$
45
46 162 were considered significant for all analyses. Adjusted odds ratio or coefficients with 95%
47
48 163 confidence intervals (CIs) were calculated. Stata 12.0 (Stata Corporation, 2012, TX)
49
50 164 statistical software was used for all analyses.
51

52 165 Ethics approval was granted through Monash University Human Research Ethics
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54 166 Committee (CF16/825-2016000402).
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167 **Results**

168 Overall, the clinical audit comprised data from 4087 patients at 112 hospitals. Most
169 were public hospitals (n=104, 93%) and were located in metropolitan areas (n=105, 94%).
170 Twenty-four of these hospitals (n=664 patients) did not have a SU. Of the patients admitted
171 to a hospital with a SU, 20% (n=684) were not treated in a SU at any time during their
172 admission. There were 2739 patients treated in a SU at some time during their admission.
173 Eighty-four patients with invalid or missing dates of admission or discharge from the hospital
174 or SU were excluded from the analyses. Overall, 2655 patients were assessed, whereby
175 almost two-thirds (64%) spent at least 90% of their admission in a SU. Supplemental Table 1
176 provides the characteristics of patients who were and were not treated in a SU at hospitals
177 with a SU. Compared to patients not treated on the SU, patients admitted in a SU were more
178 likely to be younger, male, independent prior to stroke and have an ischemic stroke
179 (Supplemental Table 1).

180 **Patient characteristics and clinical processes**

181 The median age for all included patients (n=2655) was 76 years (Q1:65, Q3:84) and
182 55% were male (Table 1 and Supplemental Table 2). Patients who spent at least 90% of their
183 admission in a SU were more likely to be younger, and have less severe strokes i.e. fewer
184 were unable to walk on admission or incontinent within 72 hours of admission compared to
185 those who spent less than 90% of their admission in a SU (Table 1).

186 Importantly, patients who spent at least 90% of their admission in a SU compared to
187 those who did not, were more likely to be admitted to a SU within three hours of arrival to
188 ED, have a brain scan within 24 hours, be discharged from the hospital on the same day they
189 were discharged from the SU (Table 1), be assessed for rehabilitation by a physiotherapist

190 within 48 hours of admission and have rehabilitation therapy commenced within 48 hours of
 191 their initial assessment (Supplemental Table 3).

192 Patients who spent at least 90% of their admission in a SU had a shorter median time
 193 (hours) from arrival to the ED to admission on a SU compared to those who spent less than
 194 90% of their admission in a SU (median time 6 hours, Q1: 4, Q3: 10 versus median time 17
 195 hours, Q1: 6, Q3: 35; $p < 0.001$).

196 **Table 1. Characteristics of patients with stroke who spent at least 90% and those who**
 197 **spent less than 90% of admission in a stroke unit**

Spent at least 90% of admission in a SU	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Patient characteristics			
Age, median (Q1, Q3) ^a	75 (65, 84)	77 (66, 85)	0.006
Male	936 (55)	537 (55)	0.99
Independent prior to stroke (mRS 0–2)	1401 (83)	810 (84)	0.68
In hospital stroke	26 (2)	37 (4)	<0.001
Stroke type			
Ischemic stroke	1426 (85)	805 (83)	0.36
Hemorrhagic stroke	162 (10)	114 (12)	0.08
Unknown stroke type	99 (6)	49 (5)	0.38
Stroke severity ^b			
Arm weakness on admission	1030 (62)	592 (63)	0.82
Impaired speech on admission	987 (60)	554 (59)	0.52
Unable to walk on admission	862 (52)	543 (57)	0.005
Incontinence at 72 hours of admission	488 (30)	340 (36)	0.001
History of comorbidities			
Atrial fibrillation ^c	418 (28)	276 (33)	0.01
Ischemic heart disease ^c	396 (27)	254 (30)	0.05
Previous stroke or TIA ^d	513 (34)	277 (32)	0.49
Clinical processes of care			
Transferred to SU within 3 hours of ED			

Spent at least 90% of admission in a SU	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
arrival ^c	229 (16)	52 (6)	<0.001
Transferred to SU within 24 hours of ED arrival ^c	1406 (95)	516 (62)	<0.001
Brain scan within 24 hrs of ED arrival ^c	1329 (97)	722 (95)	0.01
Date of discharge from SU same as date of discharge from hospital	1567 (99)	456 (52)	<0.001
Organizational characteristics			
Metropolitan hospital	1634 (97)	955 (99)	0.004
Private hospital	116 (7)	94 (10)	0.01
Stroke care coordinator present	1030 (61)	550 (57)	0.03
Access to onsite neurosurgery	566 (34)	402 (42)	<0.001
Stroke team involved in quality improvement in last 2 years	1507 (89)	831 (86)	0.008
Access to early supported discharge team	229 (14)	102 (11)	0.02
Regular multi-disciplinary team meetings	1659 (98)	941 (97)	0.05
Number of beds on SU			
<5	752 (45)	464 (48)	0.001
5-9	462 (27)	307 (32)	
≥10	473 (28)	197 (20)	
Stroke admissions last year ≥100	1563 (93)	916 (95)	0.05
Stroke specialist research nurse involved with treatment	319 (19)	140 (14)	0.004
Access to ongoing inpatient rehabilitation	1554 (92)	916 (95)	0.01
In-hospital outcomes			
Any severe complication ^f	133 (8)	129 (14)	<0.001
Independent on discharge (mRS 0-2)	845 (54)	408 (47)	0.002
Died in hospital	107 (6)	95 (10)	0.001
Discharge destination (survivors)			
Private residence	869 (55)	453 (52)	0.14

Spent at least 90% of admission in a SU	Yes	No	p-value
	(N= 1687)	(N=968)	
	n (%)	n (%)	
Residential aged care facility	74 (5)	77 (9)	<0.001
Inpatient rehabilitation	487 (31)	268 (31)	0.95
Other hospital ward	122 (8)	54 (6)	0.16
Other	28 (2)	21 (2)	0.28

198 Q1: 1st quartile; Q3: 3rd quartile; ED: emergency department; SU: stroke unit; mRS:
 199 modified Rankin scale. TIA: transient ischemic attack; ^a<1% unknown/not documented data;
 200 ^b1-5% unknown/not documented data; ^c11-15% unknown/not documented data; ^d6-10%
 201 unknown/not documented data; ^e16-20% unknown/not documented data; ^fa complication
 202 considered incapacitating, life threatening and one that prolongs hospital admission e.g.
 203 pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis etc.

204

205 In-hospital outcomes and complications

206 Complications such as aspiration pneumonia, fever, urinary tract infections, falls,
 207 stroke progression and seizures were less common in patients who spent at least 90% of their
 208 admission in a SU compared to those who spent less time in a SU (Fig 1).

209

210 The median LOS (days) in the hospital for patients who spent at least 90% of their
 211 admission in a SU was significantly shorter than those who spent less than 90% of their
 212 admission in a SU (median LOS 4, Q1: 3, Q3: 8 versus median LOS 7, Q1: 4, Q3: 13;
 213 $p < 0.001$). Patients who spent at least 90% of their admission in a SU were more likely to be
 214 independent on discharge and less likely to have any severe complication or die in the
 215 hospital (Table 1).

216 On adjustment for confounding variables, no differences were detected in
 217 independence at discharge or death between the two groups (Table 2). However, patients who
 218 spent at least 90% of their admission in a SU were 0.60 times less likely to have any severe
 219 complication and 0.59 times less likely to be discharged to a residential aged care facility
 220 than those who spent less than 90% of admission in a SU (Table 2). Median LOS for patients
 221 who spent at least 90% of their admission in a SU was two days shorter than for those who
 222 did not.

223 **Table 2. Adjusted odds ratios/coefficients for in-hospital outcomes for patients who**
 224 **spent at least 90% of their admission in a stroke unit**

Model	Outcome	aOR ^a	95% CI	p value
1.	Any severe complication ^b	0.60	0.43, 0.84	0.003
2.	Independent on discharge (mRS 0-2)	1.19	0.92, 1.53	0.19
3.	Died	0.72	0.49, 1.06	0.09
4.	Discharged to private residence	1.05	0.84, 1.32	0.67
5.	Discharged to inpatient rehabilitation	0.97	0.76, 1.23	0.79
6.	Discharged to residential aged care facility	0.59	0.38, 0.94	0.03
		Coefficient^a	95% CI	p value
7.	Length of stay (discharged)	-2.77	-3.45, -2.10	<0.001
8.	Length of stay (died)	-1.33	-5.14, 2.48	0.49
9.	Length of stay (discharged + died)	-2.88	-3.42, -2.35	<0.001

225 aOR: adjusted odds ratio; CI: confidence interval. ^aModels adjusted for age, sex, premorbid
 226 function, stroke type, stroke severity and past history of atrial fibrillation. ^ba complication
 227 considered incapacitating, life threatening and one that prolongs hospital admission e.g.
 228 pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis etc.

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3 229 Sensitivity analyses, including other cut offs for percentage of admission spent in a
4
5 230 SU (e.g. ≥ 50 to < 60 , ≥ 60 to < 70 , ≥ 70 to < 80 , ≥ 80 to < 90), provided evidence of a potential
6
7 231 dose effect between occurrence of any severe complications and percentage of admission
8
9 232 spent in a SU. In this analysis, in comparison to other cut offs of percentage of admission
10
11 233 spent in a SU, spending at least 90% of admission in a SU was associated with fewer severe
12
13 234 complications than spending less than 50% of admission in a SU ($p < 0.001$; Supplemental
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15
16 235 Table 4).

236 **Organizational characteristics**

237 Hospitals with onsite neurosurgery services, located in metropolitan areas or those
238 that were private less often kept their patients in the SU for at least 90% of their admission
239 (Table 1, Supplemental Table 2). Features of hospitals that were able to provide access to the
240 SU for at least 90% of the patient's admission included those with: at least 10 beds in a SU, a
241 SU coordinator, access to early supported discharge team, a stroke specialist research nurse
242 involved in treatment and those in which the stroke team was involved in quality
243 improvement in the previous two years (Table 1).

244 **Factors associated with spending at least 90% of admission in a** 245 **SU**

246 In multivariable analysis, similar factors remained relevant for likelihood of spending
247 at least 90% of admission in a SU (Table 3). For instance, patients who were admitted to a
248 SU within three hours of arrival to the ED were three times more likely to spend at least 90%
249 of their admission in a SU compared to those who were admitted after three hours of arrival
250 to the ED (Table 3). This finding was also similar for patients admitted in a SU within 24
251 hours of arrival to the ED (aOR: 26.17, 95% CI: 17.08, 40.09). Patients who were admitted to
252 a hospital with at least 10 beds on the SU were more likely to spend at least 90% of

253 admission in a SU compared to those admitted to a hospital with less than five beds on the
254 SU.

255 **Table 3. Factors associated with patients with stroke spending at least 90% of their**
256 **admission in a stroke unit**

Factors	OR ^a	95% CI	p value
Age			
<65	1.00		
65-74	1.11	0.78, 1.59	0.56
75-84	0.94	0.67, 1.33	0.73
≥85	0.92	0.63, 1.35	0.68
Unable to walk on admission	0.75	0.57, 0.99	0.04
Incontinent at 72 hours of admission	0.84	0.63, 1.12	0.24
History of atrial fibrillation	1.00	0.76, 1.33	0.98
History of ischemic heart disease	0.87	0.66, 1.13	0.30
Any severe complication ^b	0.64	0.43, 0.96	0.03
Stroke occurred while patient was in hospital	0.21	0.08, 0.56	0.002
Transferred to SU within 3 hours of ED arrival	3.41	2.14, 5.42	<0.001
Brain scan assessment within 24 hrs of ED arrival	2.03	1.08, 3.81	0.03
Treated in a metropolitan hospital	0.70	0.13, 3.78	0.68
Treated in a private hospital	0.77	0.33, 1.80	0.55
Stroke care coordinator present	1.42	0.91, 2.22	0.12
Treated in a hospital with onsite neurosurgery	0.49	0.30, 0.80	0.005
Stroke team involved in quality improvement in last 2 years	1.19	0.62, 2.31	0.60
Access to early supported discharge team	1.66	0.83, 3.29	0.15
Regular multi-disciplinary team meetings	1.51	0.36, 6.42	0.57
Number of beds on SU			
<5	1.00		
5-9	1.25	0.75, 2.09	0.39
≥10	1.91	1.08, 3.35	0.03
Stroke admissions last year ≥100	0.55	0.22, 1.33	0.18
Stroke specialist research nurse involved with treatment	1.52	0.80, 2.91	0.20
Access to ongoing inpatient rehabilitation	1.02	0.38, 2.69	0.97

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3 257 OR: odds ratio; CI: confidence interval; ED: emergency department; SU: stroke unit. ^a
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5 258 Multivariable model adjusted for all factors listed in table; level was hospital. ^{b a}
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7 259 complication considered incapacitating, life threatening and one that prolongs hospital
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9 260 admission e.g. pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis
10
11 261 etc.

14 262 **Discussion**

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17 263 To our knowledge, this is the first study to describe whether the recommendation for
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19 264 patients with stroke to spend at least 90% of their admission in a SU is a relevant indicator of
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21 265 high quality stroke care. We demonstrated that patients who spent at least 90% of their
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23 266 admission in a SU had a shorter LOS, experienced fewer severe complications and were less
24
25 267 often discharged to a residential aged care facility. Spending at least 90% of admission in a
26
27 268 SU was associated with fewer severe complications compared to lower proportions of time
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29 269 spent in a SU and these data provide support for the 90% benchmark. While results are based
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31 270 on stroke care provided in Australian hospitals, these findings are important for promoting
32
33 271 and ensuring that patients with stroke spend most of their acute hospital stay in a SU.

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35 272 While researchers have demonstrated that management of patients in a SU is
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37 273 associated with a reduction in length of hospital stay compared to other wards,^{13, 14} our
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39 274 findings have further demonstrated that length of time spent in a SU may also be important.
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41 275 Given the demands for beds in SUs,¹⁴ the two day reduction in LOS observed in our study is
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43 276 clinically important. Additionally, from an economic perspective, this reduction in LOS
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45 277 translates to potentially large cost-savings.¹⁵ This finding together with other improved
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47 278 outcomes such as the reduced likelihood of severe complications and discharge to residential
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49 279 aged care facility and trend towards reduced mortality for patients who spent at least 90% of
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3 280 admission in a SU provide further support for ensuring that all patients with stroke spend
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5 281 most of their acute admission in a SU.

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7 282 Given that spending at least 90% of admission in a SU influences outcomes, we have
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9 283 further demonstrated factors that are responsible for achieving this indicator. The main
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11 284 finding is that being admitted to a SU within three hours of arrival to the ED was
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13 285 independently associated with spending at least 90% of admission in a SU. This finding is of
14
15 286 great importance because early admission to a SU has also been associated with better
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17 287 recovery.¹⁶ Given evidence that SU care significantly reduces death and disability after
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19 288 stroke,^{3,4} and that the clinical guidelines for management of stroke recommend direct or early
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21 289 admission to a SU,⁵ our finding provides further evidence that early admission on a SU
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23 290 should be a high priority for clinicians and health administrators. Unfortunately, overall
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25 291 access to SU in different countries remains highly variable. For example, in Australia only 67%
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27 292 of the patients with stroke received SU care in 2015.⁷ This is a major difference to countries
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29 293 like the United Kingdom (UK) where 96% of patients received SU care.⁸ There is need to
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31 294 improve access as well as timely admission to a SU.

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35 295 Additionally, having a brain scan within 24 hours of arrival to the ED was associated
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37 296 with spending at least 90% of admission in a SU. An early brain scan is important for
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39 297 confirming the type of stroke and to exclude stroke mimics, thus enabling commencement of
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41 298 time-dependent therapies.⁵ The fact that patients who spent at least 90% of their admission in
42
43 299 a SU were more likely to begin rehabilitation therapy within 48 hours of initial assessment
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45 300 highlights the importance of this indicator. These findings provide impetus for early
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47 301 assessment and early admission of all stroke patients onto a SU as this may help to advocate
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49 302 for patients to spend most of their acute hospital stay in a SU.

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52 303 Another important finding of this study is that individuals with severe stroke (unable
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54 304 to walk on admission) and those who developed severe complications were less likely to

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3 305 spend at least 90% of their admission in a SU. This finding is important given evidence that
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5 306 SU care reduces mortality through prevention and treatment of infection and immobility-
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7 307 related complications.¹⁷ Clinicians should be informed and encouraged to admit early and
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9 308 retain in a SU this group of patients that are at greater risk of poor health outcomes, as they
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11 309 may benefit from the inter-disciplinary treatment approach offered in a SU. Because patients
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13 310 with severe stroke or those with any severe complication were less likely to be treated in a
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15 311 SU, it is possible that these patients may be admitted to other wards such as the intensive care
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17 312 unit (ICU) instead of admission on a SU.

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20 313 Having at least 10 beds on the SU was associated with spending at least 90% of
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22 314 admission in a SU and this finding provides a strong argument for capacity building and
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24 315 potential redistribution of resources within hospitals to better support care for patients with
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26 316 stroke where there is the relevant throughput of patients.⁷

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29 317 There are some limitations that must be acknowledged. The time for discharge from
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31 318 the SU and hospital was unavailable. Therefore, our analysis was limited to dates which do
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33 319 not provide fine granularity that time would have provided. Also some observations were
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35 320 excluded because of invalid or missing dates. Data on patients' ward of first admission were
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37 321 not collected which precludes us from making definitive conclusions such as whether
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39 322 individuals with severe stroke or who suffer severe complications are admitted or transferred
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41 323 to the ICU or other high dependency units first before admission on a SU or during the acute
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43 324 stay. This would have provided insight to why patients with severe complications were less
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45 325 likely to spend at least 90% of their admission in a SU. Given these limitations and the nature
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47 326 of the study design which precludes us from drawing firm conclusions about temporal
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49 327 relationships, these findings should be interpreted with caution. The above limitations
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51 328 notwithstanding, a strength of our study is the large data set from a wide cross-section of
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53 329 Australian hospitals which provides national representation.
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330 **Conclusions**

331 Spending at least 90% of time in a SU is a useful measure of care quality and was
332 associated with better patient outcomes such as shorter LOS, fewer severe complications and
333 less discharge to aged care facilities. Our findings have important implications for clinical
334 practice and development of new models of stroke care. While we have achieved direct
335 access to computed tomography from ambulance arrival with introduction of 'Code Stroke',
336 ¹⁸ consideration of the added benefits for patients of direct admissions to stroke units is
337 warranted.

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341 hospitals participating in the National Stroke Audit and all the clinicians who contributed to
342 data collection over the audit cycles.

343 **Disclosures**

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351

352 **Authors and individual contributions**

353 DB: drafting of the manuscript, performed the data analyses and contributed to the interpretation of

354 the data

355 MK: contribution to data analysis methods, manuscript revisions and interpretation of the data

356 TP: contribution to data analysis methods, manuscript revisions and interpretation of the data

357 JK: contribution to data analysis methods, manuscript revisions and interpretation of the data

358 SM: contribution to manuscript revisions

359 BC: contribution to manuscript revisions

360 DC: contribution to the supervision of analysis, interpretation of the data, manuscript revision

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362 **Data Sharing Statement**

363 Contact can be made with the corresponding author for queries relating to unpublished data.

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3 420 **Figure Legend**
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7 421 **Figure 1. Differences in complications between patients who spent at least 90% and**
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9 422 **those who spent less than 90% of their admission in a stroke unit.**

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11 423 *significant $p < 0.05$; ^aasymptomatic hemorrhagic transformation.
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21 426 **Supplemental information**
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23 427 Supplemental Table 1. Characteristics of patients with stroke treated in a stroke unit versus
24 428 those not treated in a stroke unit

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27 429 Supplemental Table 2. Characteristics of patients with stroke who spent at least 90% and
28 430 those who spent less than 90% of admission in a stroke unit

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31 431 Supplemental Table 3. Adherence to processes of care for patients who spent at least 90%
32 432 and those who spent less than 90% of hospital stay in a stroke unit

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35 433 Supplemental Table 4. Association between percentages of hospital stay spent in a stroke unit
36 434 and in-hospital outcomes of patients with stroke
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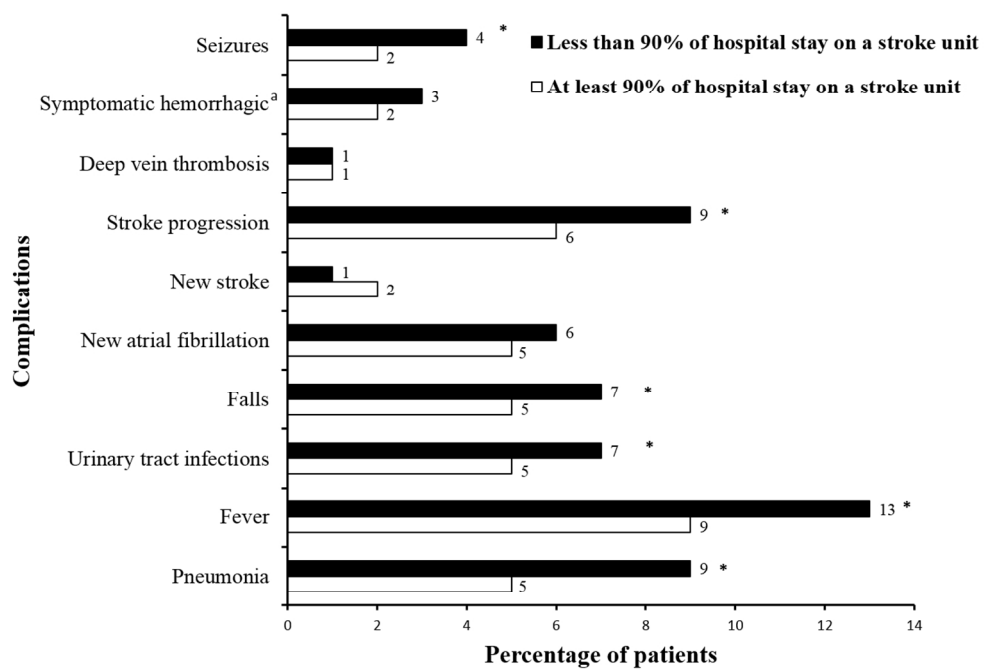


Figure 1. Differences in complications between patients who spent at least 90% and those who spent less than 90% of their admission in a stroke unit

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Supplemental Table 1. Characteristics of patients with stroke treated in a stroke unit versus those not treated in a stroke unit

Treated in a stroke unit	Yes (N= 2739) n (%)	No (N=684) n (%)	p-value
Patient characteristics			
Age, median (Q1, Q3)	76 (65, 84)	77 (65, 86)	0.03
Male	1530 (56)	347 (51)	0.02
Living at home prior to stroke	2522 (92)	586 (86)	<0.001
Independent prior to stroke (mRS 0–2)	2280 (83)	496 (73)	<0.001
In hospital stroke	75 (3)	54 (8)	<0.001
Stroke type			
Ischemic stroke	2302 (84)	449 (66)	<0.001
Hemorrhagic stroke	286 (10)	163 (24)	<0.001
Unknown stroke type	151 (6)	72 (11)	<0.001
Stroke severity			
Arm weakness on admission	1675 (62)	352 (59)	0.18
Impaired speech on admission	1582 (59)	333 (57)	0.43
Unable to walk on admission	1454 (54)	392 (59)	0.02
Incontinence at 72 hours of admission	857 (32)	258 (42)	<0.001
History of comorbidities			
Atrial fibrillation			
Hypercholesterolemia	1058 (44)	225 (43)	0.73
Hypertension	1820 (70)	419 (70)	0.92
Diabetes mellitus	669 (27)	160 (29)	0.36
Ischemic heart disease	670 (28)	175 (33)	0.02
Previous stroke or TIA	814 (33)	221 (39)	0.007
Organizational characteristics			
Metropolitan hospital	2672 (98)	661 (97)	0.18
Private hospital	217 (8)	37 (5)	0.03
Stroke care coordinator present	1626 (59)	446 (65)	0.005
Access to onsite neurosurgery	1000 (37)	210 (31)	0.004
Dedicated multi-disciplinary team present	2706 (99)	677 (99)	0.69
ED protocols for rapid triage	2625 (96)	643 (94)	0.04
Access to on site MRI within 24 hours	2136 (78)	517 (76)	0.18
Stroke team involved in quality improvement in last 2 years	2416 (88)	543 (79)	<0.001
Clinical care pathways for managing stroke present	2339 (85)	569 (83)	0.15
Access to early supported discharge team	338 (12)	103 (15)	0.06
Patients given discharge care plan	1275 (47)	347 (51)	0.05
Regular multi-disciplinary team meetings	2683 (98)	665 (97)	0.24
Arrangements with ambulance for rapid transfers	1897 (73)	498 (78)	0.003
Offering thrombolysis	2404 (88)	606 (89)	0.55
Program for continuing education of staff	2609 (95)	649 (95)	0.69
Number of beds on SU			<0.001

Treated in a stroke unit	Yes (N= 2739) n (%)	No (N=684) n (%)	p-value
<5	1246 (45)	380 (56)	
5-9	790 (29)	179 (26)	
≥10	703 (26)	125 (18)	
Stroke admissions last year ≥100	2558 (93)	602 (88)	<0.001
CT scanning within 3 hours for all patients	2690 (98)	676 (99)	0.26
Clinical processes of care			
Brain scan within 24 hrs of ED arrival	2108 (96)	496 (96)	0.35
Assessment in the ED	1071 (44)	127 (28)	<0.001
Time-critical therapy			
Thrombolysis in ischemic stroke (with exclusions)	198 (10)	24 (6)	0.01
Assessment for rehabilitation by a physiotherapist within 24-48 hours of hospital admission	1605 (59)	198 (29)	<0.001
Rehabilitation therapy within 48 hours of initial assessment	1899 (89)	249 (67)	<0.001
Transition from hospital care			
Written care plan	1113 (61)	192 (48)	<0.001
Outcomes			
Any severe complication ^a	277 (10)	135 (20)	<0.001
Independent on discharge (mRS 0-2)	1285 (51)	263 (51)	0.84
Died in hospital	207 (8)	170 (25)	<0.001
Discharge destination (survivors)			
Private residence	1350 (53)	293 (57)	0.13
Residential aged care facility	156 (6)	43 (8)	0.07
Inpatient rehabilitation	785 (31)	77 (15)	<0.001
Other hospital ward	191 (8)	90 (18)	<0.001
In-hospital complications			
Aspiration Pneumonia	183 (7)	45 (7)	0.92
Falls	167 (6)	26 (4)	0.02
Fever	289 (11)	75 (11)	0.75
Urinary tract infections	169 (6)	30 (4)	0.07
New stroke	47 (2)	38 (6)	<0.001
Stroke progression	187 (7)	82 (12)	<0.001
New onset atrial fibrillation	155 (6)	28 (4)	0.10
Symptomatic hemorrhagic transformation	73 (3)	26 (4)	0.11
Deep vein thrombosis	15 (1)	4 (1)	0.91
Seizures	67 (2)	34 (5)	<0.001

Q1: 1st quartile; Q3: 3rd quartile; ED: emergency department; SU: stroke unit; mRS: modified Rankin scale. TIA: transient ischaemic attack; MRI: magnetic resonance imaging; ^aa complication considered incapacitating, life threatening and one that prolongs hospital admission and patient acuity including pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis etc.

Supplemental Table 2. Characteristics of patients with stroke who spent at least 90% and those who spent less than 90% of admission in a stroke unit

Spent at least 90% of admission in a stroke unit	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Patient characteristics			
Living at home prior to stroke	1543 (91)	898 (93)	0.24
Arrived by ambulance ^a	1145 (76)	678 (79)	0.21
History of comorbidities			
Hypercholesterolemia ^a	653 (44)	366 (43)	0.69
Hypertension ^b	1123 (70)	644 (71)	0.76
Diabetes mellitus ^c	401 (26)	253 (29)	0.14
Previous stroke or TIA ^c	513 (34)	277 (32)	0.49
Clinical processes of care			
Brain scan within 3 hrs of ED arrival ^d	1053 (77)	567 (75)	0.24
Organizational characteristics			
Dedicated multi-disciplinary team present	1669 (99)	953 (98)	0.28
ED protocols for rapid triage	1626 (96)	919 (95)	0.07
Access to on site MRI within 24 hours	1306 (77)	765 (79)	0.33
Clinical care pathways for managing stroke present	1452 (86)	827 (85)	0.65
Patients given discharge care plan	772 (46)	464 (48)	0.28
Arrangements with ambulance for rapid transfers	1163 (73)	675 (73)	0.90
Offering thrombolysis	1490 (88)	838 (87)	0.19
Standardized processes to assess rehabilitation	1346 (80)	749 (77)	0.14
Program for continuing education of staff	1603 (95)	926 (96)	0.46
Neurologist involved in stroke management	1224 (73)	720 (74)	0.31
CT scanning within 3 hours for all patients	1651 (98)	955 (99)	0.15

ED: emergency department; TIA: transient ischemic attack; CT: computed tomography; ^a11-15% unknown/not documented data; ^b1-5% unknown/not documented data; ^c6-10% unknown/not documented data; ^d16-20% unknown/not documented data.

Supplemental Table 3. Adherence to processes of care for patients who spent at least 90% and those who spent less than 90% of hospital stay in a stroke unit

Spent at least 90% of hospital stay in a stroke unit	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Early assessment			
Assessment in the ED	675 (44)	367 (43)	0.79
Time-critical therapy			
Transport by ambulance to hospital able to provide thrombolysis	1015 (76)	597 (79)	0.23
Thrombolysis in ischemic stroke (with exclusions) ^a	99 (8)	94 (13)	<0.001
Thrombolysis in ischemic stroke for those who arrive within 4.5 hours of symptom onset	88 (25)	83 (36)	0.003
Thrombolysis within 60 minutes of hospital arrival	32 (32)	20 (21)	0.08
Time (median) from onset of symptoms to thrombolysis (Q1,Q3)	2.8 (1.9, 3.7)	3 (2.3, 3.8)	0.10
Early rehabilitation			
Assessment for rehabilitation by a physiotherapist within 24-48 hours of hospital admission ^b	1185 (70)	643 (66)	0.04
Rehabilitation therapy within 48 hours of initial assessment	1161 (90)	673 (86)	0.01
Treatment for a rehabilitation goal commencing during an acute hospital admission	1256 (94)	738 (92)	0.14
Minimising risk of another stroke			
Discharge on antihypertensive medication ^c	701 (75)	404 (77)	0.54
Discharge on statin, antihypertensive and antithrombotic medications (ischemic stroke) ^d	526 (66)	285 (66)	0.84
Discharge on oral anticoagulants for atrial fibrillation (ischemic stroke)	144 (68)	87 (63)	0.38
Risk factor modification advice before leaving hospital	597 (61)	353 (64)	0.32
Carer training and support			
Carer support needs assessment	113 (64)	79 (72)	0.13
Carer training	99 (55)	58 (56)	0.87
Transition from hospital care			
Written care plan	699 (62)	377 (59)	0.16

ED: emergency department; Q1: 1st quartile; Q3: 3rd quartile; SU: stroke unit; ^a patients with premorbid functional impairment, recent surgery, major comorbidity, warfarin with INR>1.7, rapidly improving, imaging showing spontaneous reperfusion, other contraindication; ^b recorded as within 48 hours; ^cexcludes those contraindicated to treatment; ^d excludes those where treatment was contraindicated or futile, or the patient refused.

Supplemental Table 4. Association between percentages of hospital stay spent in a stroke unit and in-hospital outcomes of patients with stroke

Model	Percentage of time spent in a SU (%)	aOR ^a	95% CI	P-value
1	Any severe Complications ^b			
	< 50	1		
	≥50 to <60	1.35	(0.68, 2.69)	0.40
	≥60 to <70	0.56	(0.23, 1.36)	0.20
	≥70 to <80	0.54	(0.23, 1.26)	0.15
	≥80 to <90	0.51	(0.25, 1.05)	0.07
	≥90	0.47	(0.30, 0.74)	0.001
2	LOS less than or equal to median LOS (5 days) - discharged			
	< 50	1		
	≥50 to <60	7.31	(4.12, 12.97)	<0.001
	≥60 to <70	9.15	(5.14, 16.27)	<0.001
	≥70 to <80	6.31	(3.52, 11.31)	<0.001
	≥80 to <90	2.27	(1.28, 4.02)	0.005
	≥90	9.71	(6.42, 14.69)	<0.001
3	Independent at discharge (mRS 0-2)			
	< 50	1		
	≥50 to <60	1.67	(0.90, 3.10)	0.10
	≥60 to <70	1.61	(0.89, 2.91)	0.11
	≥70 to <80	2.02	(1.08, 3.79)	0.03
	≥80 to <90	1.07	(0.60, 1.90)	0.82
	≥90	1.57	(1.07, 2.28)	0.02

SU: stroke unit; aOR: adjusted odds ratio; CI: confidence interval; LOS: length of stay; mRS: modified Rankin scale. ^aModels adjusted for age, gender, pre-morbid function, stroke type, stroke severity and past history of atrial fibrillation. ^ba complication considered incapacitating, life threatening and one that prolongs hospital admission and patient acuity including pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis etc.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found (Page 2)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (Page 4)
Objectives	3	State specific objectives, including any prespecified hypotheses (Page 4)
Methods		
Study design	4	Present key elements of study design early in the paper (Page 4)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (Page 5)
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants (Page 5)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (Page 5 & 6)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (Page 5 & 6)
Bias	9	Describe any efforts to address potential sources of bias (Page 6 & 7)
Study size	10	Explain how the study size was arrived at (Page 5)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (Page 5 & 6)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (Page 6 & 7) (b) Describe any methods used to examine subgroups and interactions (Page 6 & 7) (c) Explain how missing data were addressed (Page 6) (d) If applicable, describe analytical methods taking account of sampling strategy (N/A) (e) Describe any sensitivity analyses (Page 7)
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (Page 8) (b) Give reasons for non-participation at each stage (N/A) (c) Consider use of a flow diagram (N/A)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (Page 8, Table 1) (b) Indicate number of participants with missing data for each variable of interest (Table 1)
Outcome data	15*	Report numbers of outcome events or summary measures (Page 11, 12, Table 2, Table 3)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (Page 11, Page 12, Page 13, Table 2,

Table 3)

		(b) Report category boundaries when continuous variables were categorized (N/A)
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period (N/A)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses (Page 13, Supplemental Table 4)
Discussion		
Key results	18	Summarise key results with reference to study objectives (Page 15)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (Page 17)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (Page 15, Page 17)
Generalisability	21	Discuss the generalisability (external validity) of the study results (Page 15)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (Page 18)

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Is length of time in a stroke unit associated with better outcomes for patients with stroke in Australia? An observational study

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Manuscripts

1 Is length of time in a stroke unit associated with better
2 outcomes for patients with stroke in Australia? An
3 observational study

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27 Abstract

28 **Objective:** Spending at least 90% of hospital admission in a stroke unit (SU) is a
29 recommended indicator of receiving high quality stroke care. However, whether this makes a
30 difference to patient outcomes is unknown. We aimed to investigate outcomes and factors
31 associated with patients with acute stroke spending at least 90% of their admission in a SU,
32 compared to those having less time in the SU.

33 **Design:** Observational study using cross-sectional data

34 **Setting:** Data from hospitals which participated in the 2015 Stroke Foundation National
35 Audit: Acute Services (Australia) and had a SU. This audit includes an organisational survey
36 and retrospective medical record audit of approximately 40 admissions from each hospital.

37 **Participants:** Patients admitted to a SU during their acute admission were included.

38 **Outcome measures:** Hospital-based patient outcomes included length of stay, independence
39 on discharge, severe complications and discharge destination. Patient, organisational, and
40 process indicators were included in multilevel logistic modelling to determine factors
41 associated with spending at least 90% of their admission in a SU.

42 **Results:** Eighty-eight hospitals with a SU audited 2655 cases (median age 76 years, 55%
43 male). Patients who spent at least 90% of their admission in a SU experienced: a length of
44 stay that was two days shorter (coefficient -2.77 95% CI -3.45, -2.10), fewer severe
45 complications (aOR: 0.60; 95% CI: 0.43, 0.84) and were less often discharged to residential
46 aged care (aOR: 0.59; 95% CI: 0.38, 0.94) than those who had less time in the SU. Patients
47 admitted to a SU within three hours of hospital arrival were three times more likely to spend
48 at least 90% of their admission in a SU.

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3 49 **Conclusion:** Spending at least 90% of time in a SU is a valid measure of stroke care quality
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5 50 as it results in improved patient outcomes. Direct admission to stroke units is warranted.
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11 52 **ARTICLE SUMMARY**
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14 53 **Strengths and limitations of this study:**
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17 54 • A strength of this research is that it has provided further evidence of the importance of
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19 55 length of time in a SU, not just access, which has implications for clinical practice and
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21 56 development of new models of stroke care.
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24 57 • The study involved a large comprehensive dataset, which provided national representation
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26 58 and utilised standardised data collection and an inclusive data dictionary to minimise
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28 59 reporting bias and ensure data were reliably collected.
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31 60 • For some outcomes, only dates, rather than times were collected, which would have
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33 61 provided more accuracy.
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36 62 • Design permits only association rather than determination of causality.
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70 **Introduction**

71 Stroke remains a major global health challenge because it is a leading cause of death
72 and major disability.¹ It is well-established that patients treated in stroke units (SUs) are more
73 likely to receive evidence-based clinical practices, have better survival and self-rated quality
74 of life compared to those receiving care in other wards.²⁻⁴ Direct admission to the SU is
75 recommended, preferably within three hours of stroke onset.⁵ Unless stroke is not a main
76 clinical problem, guidelines also recommend that patients should be treated in a SU
77 throughout their entire admission.⁶ Various factors can affect the time that patients spend in a
78 SU. These factors include the bed capacity of the SU,⁷ bed management decisions,^{8,9} hospital
79 policies, delays in the emergency department,¹⁰ the clinical acuity of the patient whereby
80 intubation or management in intensive care is warranted,¹¹ or delayed discharges for the next
81 stage of care (e.g. inpatient rehabilitation, or aged care facility). Within Australia and in other
82 counties, it has been recommended that ‘spending at least 90% of the hospital admission in a
83 SU’ is an important indicator of high quality acute stroke care.¹²⁻¹⁴ However, there is limited
84 evidence that the proportion of time spent in the SU is associated with better outcomes in
85 patients with stroke. In an observational study using data from the United Kingdom National
86 Sentinel Audit of Stroke, lower case fatality was associated with spending more than 50% of
87 hospital stay in the SU.¹⁵ Specific evidence is lacking relating to the benefits of spending 90%
88 or more of the admission in a SU. In our study, we aimed to investigate in-hospital patient
89 outcomes, and determine factors associated with patients with acute stroke spending at least
90 90% of their admission in a SU, compared to those having less time in the SU.

91 **Materials and methods**

92 The description and reporting of this study is based on the Strengthening the
93 Reporting of Observational Studies in Epidemiology (STROBE) statement.¹⁶

94 **Context of acute stroke care**

95 In Australia, the majority of patients with stroke are managed in public hospitals. It is
96 usual practice that patients with suspected stroke or transient ischaemic attack present to the
97 emergency department of hospitals, and are rapidly assessed, with brain imaging performed
98 as a priority. Generally, all patients should be admitted to an acute SU, or medical ward if the
99 hospital has no available beds in the SU or does not have a SU or neurology ward. If patients
100 require intubation or require higher acuity monitoring and one-to-one nursing care, they may
101 also be managed in an intensive care unit. The median length of stay in the acute setting is 5
102 days (Q1, 2; Q3, 8),¹⁷ after which, if rehabilitation is required, it is either provided in a
103 separate subacute rehabilitation ward or hospital, or in a community setting.

104 **Study design and data source**

105 This observational study used data from hospitals participating in the Australian
106 Stroke Foundation Acute Services Audit Program conducted in 2015. The audit program is
107 run biennially to provide cross-sectional data on clinical performance, and has two
108 components: an organisational survey and clinical audit.¹⁸ Detailed methods for the Audit
109 Program have been described elsewhere.¹⁸ In brief, data obtained in the organisational survey
110 are used to describe aspects of acute stroke services, including bed numbers, admissions per
111 year and available resources e.g. stroke units. Data collected in the clinical audit are used to
112 identify adherence to clinical guidelines and provide evidence on areas to improve the quality
113 of care. Participation in the audit was voluntary and all Australian acute stroke services
114 admitting at least three acute stroke patients per year were eligible to participate. Data for the
115 first 40 or more consecutive acute stroke admissions (from 1 September 2014 and discharged
116 by 28 February 2015) were collected by trained data abstractors from June to August 2015.
117 To obtain a more representative sample, larger hospitals were encouraged to provide more

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3 118 cases. Patients with a primary diagnosis of acute stroke (ICD-10 codes: I61, I62.9, I63, I64)
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5 119 were eligible to be included in the audit.
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7 120 **Patient population and definitions**

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10 121 Data for patients who were treated at a hospital with a SU and only those patients
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12 122 admitted to a SU during their acute admission were included. Time spent in a SU (SU time)
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14 123 was determined by subtracting the date of discharge from the SU, from the date of admission
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16 124 to the SU. To determine patients who spent at least 90% of their admission in a SU, the SU
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18 125 time was divided by total length of stay (LOS) in the hospital (total LOS; calculated by
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20 126 subtracting date of discharge from hospital or death from date of admission to hospital. This
21
22 127 corresponds to the admission to the respective acute care ward, or commencement of an
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24 128 episode of care) and the result multiplied by one hundred ($[\text{SU time}/\text{total LOS}] * 100$). We
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26 129 further determined early/late admission to the SU as ≤ 3 hours versus > 3 hours from arrival to
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28 130 the emergency department (ED) to admission on the SU. For patients whose stroke occurred
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30 131 while they were already in hospital, date of stroke onset was used as a surrogate for date of
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32 132 admission to hospital and arrival to ED.
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36 133 The following patient outcomes were assessed: LOS, death, level of independence on
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38 134 discharge, severe complications and discharge destination. LOS was defined as the total
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40 135 length of time from admission to the hospital to discharge from the hospital or death. Level of
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42 136 independence on discharge was defined as a modified Rankin scale (mRS) score of zero to
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44 137 two. A severe complication was a new event in hospital considered to be incapacitating, life
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46 138 threatening and one that prolonged hospital admission such as pneumonia, falls, fever,
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48 139 urinary tract infection, seizures and deep vein thrombosis. Discharge destinations included
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50 140 private residence, inpatient rehabilitation or residential aged care facility.
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53 141 Only valid yes/no responses were included in the analyses for data related to medical
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55 142 history and the presence of symptoms on presentation to hospital. For data relating to
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3 143 processes of care, e.g. received care in a SU, not documented and unknown responses were
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5 144 assumed to be negative and included in the denominator. To minimise bias, only patients with
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7 145 valid admission and discharge (SU and hospital) time or date were included.
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9 146 **Statistical analysis**

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12 147 Univariable analyses were performed to determine differences between patients who
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14 148 spent at least 90% and those who spent less than 90% of their admission in a SU. The chi-
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16 149 square test was used for categorical variables. The nonparametric Wilcoxon Mann-Whitney
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18 150 rank sum test was used for continuous variables that were not normally distributed.
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21 151 Multilevel random effects logistic regression analyses, with level defined as hospital
22
23 152 were undertaken to determine:

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25 153 i) the association between spending at least 90% of admission in a SU and in-
26
27 154 hospital outcomes such as death, level of independence on discharge (mRS 0-2),
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29 155 severe complications and various discharge destinations.
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31
32 156 ii) factors associated with spending at least 90% of the admission in a SU.
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35 157 For the continuous outcome of LOS, a median regression model with bootstrap
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37 158 estimated standard errors was undertaken. A parsimonious approach to multivariable model
38
39 159 development was used and independent variables with statistical significance ($p \leq 0.05$) from
40
41 160 univariable analyses were included.
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44 161 To determine factors associated with spending at least 90% of the admission in a SU,
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46 162 independent variables considered for inclusion in multivariable analyses were patient factors
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48 163 e.g. age; health system factors e.g. private hospital, presence of a stroke care coordinator and
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50 164 onsite neurosurgery; and clinical process factors e.g. admission to SU within three hours of
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52 165 arrival to ED. Other potential confounders including stroke type (ischaemic vs intracerebral
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54 166 haemorrhage and unknown) and stroke severity factors such as inability to walk, arm
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3 167 weakness, and speech impairment on admission and incontinence within 72 hours, which are
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5 168 based on the Counsell et al validated prognostic model for comparing patient outcomes,¹⁹
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7 169 were included. This validated model¹⁹ has been compared against a model using age plus
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9 170 scores on the National Institutes of Health Stroke Scale and both prognostic models
10
11 171 performed well overall, thus the choice between them should be based on clinical and
12
13 172 practical considerations.²⁰

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16 173 Models for association between length of time spent in a SU and in-hospital outcomes
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18 174 were adjusted for patient characteristics (e.g. premorbid function and past history of atrial
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20 175 fibrillation), variables with clinical importance (e.g. sex and age), stroke type and stroke
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22 176 severity factors. Additional sensitivity analyses were undertaken, including:

- 24 177 i) propensity score matching with stratification to minimise potential
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26 178 confounding by indication and compare between similar subgroups of patients
27
28 179 (see Supplemental Methods).
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31 180 ii) other cut offs for percentage of admission spent in a SU (e.g. ≥ 50 to <60 , \geq
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33 181 60 to <70 , ≥ 70 to <80 , ≥ 80 to <90) were undertaken to determine a potential
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35 182 dose effect with LOS, severe complications, and independence on discharge.
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38 183 Standard techniques were implemented to check for collinearity. Values of $p < 0.05$
39
40 184 were considered significant for all analyses. Adjusted odds ratio or coefficients with 95%
41
42 185 confidence intervals (CIs) were calculated. Stata 12.0 (Stata Corporation, 2012, TX)
43
44 186 statistical software was used for all analyses.
45

46 187 Ethics approval was granted through Monash University Human Research Ethics
47
48 188 Committee (CF16/825-2016000402).
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51 189 **Patient and Public Involvement**

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54 190 Patients and/or the public were not involved in the development of this research
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56 191 project.
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192 **Results**

193 Overall, the clinical audit comprised data from 4087 patients at 112 hospitals. Most
194 were public hospitals (n=104, 93%) and were located in metropolitan areas (n=105, 94%).
195 Twenty-four of these hospitals (n=664 patients) did not have a SU. Of the patients admitted
196 to a hospital with a SU, 20% (n=684) were not treated in a SU at any time during their
197 admission. There were 2739 patients treated in a SU at some time during their admission.
198 Eighty-four patients with invalid or missing dates of admission or discharge from the hospital
199 or SU were excluded from the analyses. Overall, 2655 patients were assessed, whereby
200 almost two-thirds (64%) spent at least 90% of their admission in a SU. Compared to patients
201 not treated on the SU, patients admitted in a SU were more likely to be younger, male,
202 independent prior to stroke and have an ischaemic stroke (Supplemental Table A).

203 **Patient characteristics and clinical processes**

204 The median age for all included patients (n=2655) was 76 years (Q1:65, Q3:84) and
205 55% were male (Table 1). Patients who spent at least 90% of their admission in a SU were
206 more likely to be younger, and have less severe strokes i.e. fewer were unable to walk on
207 admission or incontinent within 72 hours of admission compared to those who spent less than
208 90% of their admission in a SU (Table 1 and Supplemental Table B).

209 Importantly, patients who spent at least 90% of their admission in a SU compared to
210 those who did not, were more likely to be admitted to a SU within three hours of arrival to
211 ED, have a brain scan within 24 hours, be discharged from the hospital on the same day they
212 were discharged from the SU (Table 1), be assessed for rehabilitation by a physiotherapist
213 within 48 hours of admission and have rehabilitation therapy commenced within 48 hours of
214 their initial assessment (Supplemental Table C).

215 Patients who spent at least 90% of their admission in a SU had a shorter median time
 216 (hours) from arrival to the ED to admission on a SU compared to those who spent less than
 217 90% of their admission in a SU (median time 6 hours, Q1: 4, Q3: 10 versus median time 17
 218 hours, Q1: 6, Q3: 35; $p < 0.001$).

219

220 **Table 1. Characteristics of patients with stroke who spent at least 90% and those who**
 221 **spent less than 90% of admission in a stroke unit**

Spent at least 90% of admission in a SU	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Patient characteristics			
Age, median (Q1, Q3) ^a	75 (65, 84)	77 (66, 85)	0.006
Male	936 (55)	537 (55)	0.99
Independent prior to stroke (mRS 0–2)	1401 (83)	810 (84)	0.68
In hospital stroke	26 (2)	37 (4)	<0.001
Stroke type			
Ischaemic stroke	1426 (85)	805 (83)	0.36
Haemorrhagic stroke	162 (10)	114 (12)	0.08
Unknown stroke type	99 (6)	49 (5)	0.38
Stroke severity ^b			
Arm weakness on admission	1030 (62)	592 (63)	0.82
Impaired speech on admission	987 (60)	554 (59)	0.52
Unable to walk on admission	862 (52)	543 (57)	0.005
Incontinence at 72 hours of admission	488 (30)	340 (36)	0.001
History of comorbidities			
Atrial fibrillation ^c	418 (28)	276 (33)	0.01
Ischaemic heart disease ^c	396 (27)	254 (30)	0.05
Previous stroke or TIA ^d	513 (34)	277 (32)	0.49
Clinical processes of care			
Transferred to SU within 3 hours of ED arrival ^c	229 (16)	52 (6)	<0.001

Spent at least 90% of admission in a SU	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Transferred to SU within 24 hours of ED arrival ^c	1406 (95)	516 (62)	<0.001
Brain scan within 24 hours of ED arrival ^c	1329 (97)	722 (95)	0.01
Date of discharge from SU same as date of discharge from hospital	1567 (99)	456 (52)	<0.001
Organisational characteristics			
Metropolitan hospital	1634 (97)	955 (99)	0.004
Private hospital	116 (7)	94 (10)	0.01
Stroke care coordinator present	1030 (61)	550 (57)	0.03
Access to onsite neurosurgery	566 (34)	402 (42)	<0.001
Stroke team involved in quality improvement in last 2 years	1507 (89)	831 (86)	0.008
Access to early supported discharge			
Team	229 (14)	102 (11)	0.02
Regular multi-disciplinary team meetings	1659 (98)	941 (97)	0.05
Number of beds on SU			
<5	752 (45)	464 (48)	0.001
5-9	462 (27)	307 (32)	
≥10	473 (28)	197 (20)	
Stroke admissions last year ≥100	1563 (93)	916 (95)	0.05
Stroke specialist research nurse involved with treatment	319 (19)	140 (14)	0.004
Access to ongoing inpatient rehabilitation	1554 (92)	916 (95)	0.01
In-hospital outcomes			
Any severe complication ^f	133 (8)	129 (14)	<0.001
Independent on discharge (mRS 0-2)	845 (54)	408 (47)	0.002
Died in hospital	107 (6)	95 (10)	0.001
Discharge destination (survivors)			
Private residence	869 (55)	453 (52)	0.14
Residential aged care facility	74 (5)	77 (9)	<0.001

Spent at least 90% of admission in a SU	Yes	No	p-value
	(N= 1687)	(N=968)	
	n (%)	n (%)	
Inpatient rehabilitation	487 (31)	268 (31)	0.95
Other hospital ward	122 (8)	54 (6)	0.16
Other	28 (2)	21 (2)	0.28

222 Q1: 1st quartile; Q3: 3rd quartile; ED: emergency department; SU: stroke unit; mRS: modified Rankin scale.
 223 TIA: transient ischaemic attack; ^a <1% unknown/not documented data; ^b 1-5% unknown/not documented data;
 224 ^c 11-15% unknown/not documented data; ^d 6-10% unknown/not documented data; ^e 16-20% unknown/not
 225 documented data; ^f a complication considered incapacitating, life threatening and one that prolongs hospital
 226 admission e.g. pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis etc.

227 In-hospital outcomes and complications

228 Complications such as aspiration pneumonia, fever, urinary tract infections, falls,
 229 stroke progression and seizures were less common in patients who spent at least 90% of their
 230 admission in a SU compared to those who spent less time in a SU (Fig 1).

232 The median LOS (days) in the hospital for patients who spent at least 90% of their
 233 admission in a SU was significantly shorter than those who spent less than 90% of their
 234 admission in a SU (median LOS 4, Q1: 3, Q3: 8 versus median LOS 7, Q1: 4, Q3: 13;
 235 $p < 0.001$). Patients who spent at least 90% of their admission in a SU were more likely to be
 236 independent on discharge and less likely to have any severe complication or die in the
 237 hospital (Table 1).

238 On adjustment for confounding variables, no differences were detected in
 239 independence at discharge or death between the two groups (Table 2). However, patients who
 240 spent at least 90% of their admission in a SU were 0.60 times less likely to have any severe
 241 complication and 0.59 times less likely to be discharged to a residential aged care facility
 242 than those who spent less than 90% of admission in a SU (Table 2). Patients discharged to

243 aged care were more likely to be transferred from the SU to another ward/unit before being
 244 discharged from hospital regardless of how long they spent in the SU (Discharged aged care:
 245 60% were discharged from the SU the same day as from hospital; other destination: 84%).

246 Median LOS for patients who spent at least 90% of their admission in a SU was two
 247 days shorter than for those who did not. No difference in median LOS between groups for
 248 those patients who suffered a severe complication was evident (Table 2). Results from the
 249 sensitivity analyses using propensity score matching provided evidence of benefit from a
 250 greater proportion of time spent in a SU when confounding by indication is controlled
 251 (Supplemental Tables D and E). These results are consistent with our findings from the
 252 primary analysis.

253
 254
 255 **Table 2. Adjusted odds ratios/coefficients for in-hospital outcomes for patients who**
 256 **spent at least 90% of their admission in a stroke unit**

Model	Outcome	aOR ^a	95% CI	p value
1.	Any severe complication ^b	0.60	0.43, 0.84	0.003
2.	Independent on discharge (mRS 0-2)	1.19	0.92, 1.53	0.19
3.	Died	0.72	0.49, 1.06	0.09
4.	Discharged to private residence	1.05	0.84, 1.32	0.67
5.	Discharged to inpatient rehabilitation	0.97	0.76, 1.23	0.79
6.	Discharged to residential aged care facility	0.59	0.38, 0.94	0.03
		Coefficient^a	95% CI	p value
7.	Length of stay (discharged)	-2.77	-3.45, -2.10	<0.001
8.	Length of stay (if severe complication)	-1.89	-8.42, 4.63	0.57

9.	Length of stay (no severe complication)	-2.58	-3.12, -2.04	<0.001
10.	Length of stay (died)	-1.33	-5.14, 2.48	0.49
11.	Length of stay (discharged + died)	-2.88	-3.42, -2.35	<0.001

257 aOR: adjusted odds ratio; CI: confidence interval. ^aModels adjusted for age, sex, premorbid function,
 258 stroke type, stroke severity and past history of atrial fibrillation. ^ba complication considered incapacitating,
 259 life threatening and one that prolongs hospital admission e.g. pneumonia, falls, fever, urinary tract
 260 infection, seizures, deep vein thrombosis etc.

261 Sensitivity analyses, including other cut offs for percentage of admission spent in a
 262 SU (e.g. ≥ 50 to < 60 , ≥ 60 to < 70 , ≥ 70 to < 80 , ≥ 80 to < 90), provided evidence of a potential
 263 dose effect between occurrence of any severe complications and percentage of admission
 264 spent in a SU. In this analysis, in comparison to other cut offs of percentage of admission
 265 spent in a SU, spending at least 90% of admission in a SU was associated with fewer severe
 266 complications than spending less than 50% of admission in a SU ($p < 0.001$; Supplemental
 267 Table F).

268 **Organisational characteristics**

269 Hospitals with onsite neurosurgery services, located in metropolitan areas or those
 270 that were private less often kept their patients in the SU for at least 90% of their admission
 271 (Table 1, Supplemental Table B). Features of hospitals that were able to provide access to the
 272 SU for at least 90% of the patient's admission included those with: at least 10 beds in a SU, a
 273 SU coordinator, access to early supported discharge team, a stroke specialist research nurse
 274 involved in treatment and those in which the stroke team was involved in quality
 275 improvement in the previous two years (Table 1).

276 **Factors associated with spending at least 90% of admission in a** 277 **SU**

278 In multivariable analysis, similar factors remained relevant for likelihood of spending
 279 at least 90% of admission in a SU (Table 3). For instance, patients who were admitted to a
 280 SU within three hours of arrival to the ED were three times more likely to spend at least 90%
 281 of their admission in a SU compared to those who were admitted after three hours of arrival
 282 to the ED (Table 3). This finding was also similar for patients admitted in a SU within 24
 283 hours of arrival to the ED (aOR: 26.17, 95% CI: 17.08, 40.09). Patients who were admitted to
 284 a hospital with at least 10 beds on the SU were more likely to spend at least 90% of
 285 admission in a SU compared to those admitted to a hospital with less than five beds on the
 286 SU.

287 **Table 3. Factors associated with patients with stroke spending at least 90% of their**
 288 **admission in a stroke unit**

Factors	OR ^a	95% CI	p value
Age			
<65	1.00		
65-74	1.11	0.78, 1.59	0.56
75-84	0.94	0.67, 1.33	0.73
≥85	0.92	0.63, 1.35	0.68
Unable to walk on admission	0.75	0.57, 0.99	0.04
Incontinent at 72 hours of admission	0.84	0.63, 1.12	0.24
History of atrial fibrillation	1.00	0.76, 1.33	0.98
History of ischaemic heart disease	0.87	0.66, 1.13	0.30
Any severe complication ^b	0.64	0.43, 0.96	0.03
Stroke occurred while patient was in hospital	0.21	0.08, 0.56	0.002
Transferred to SU within 3 hours of ED arrival	3.41	2.14, 5.42	<0.001
Brain scan assessment within 24 hours of ED arrival	2.03	1.08, 3.81	0.03
Treated in a metropolitan hospital	0.70	0.13, 3.78	0.68
Treated in a private hospital	0.77	0.33, 1.80	0.55
Stroke care coordinator present	1.42	0.91, 2.22	0.12
Treated in a hospital with onsite neurosurgery	0.49	0.30, 0.80	0.005
Stroke team involved in quality improvement in last 2 years	1.19	0.62, 2.31	0.60

Access to early supported discharge team	1.66	0.83, 3.29	0.15
Regular multi-disciplinary team meetings	1.51	0.36, 6.42	0.57
Number of beds on SU			
<5	1.00		
5-9	1.25	0.75, 2.09	0.39
≥10	1.91	1.08, 3.35	0.03
Stroke admissions last year ≥100	0.55	0.22, 1.33	0.18
Stroke specialist research nurse involved with treatment	1.52	0.80, 2.91	0.20
Access to ongoing inpatient rehabilitation	1.02	0.38, 2.69	0.97

289 OR: odds ratio; CI: confidence interval; ED: emergency department; SU: stroke unit. ^a Multivariable model
 290 adjusted for all factors listed in table; level was hospital. ^b a complication considered incapacitating, life
 291 threatening and one that prolongs hospital admission e.g. pneumonia, falls, fever, urinary tract infection,
 292 seizures, deep vein thrombosis etc.

293 Discussion

294 To our knowledge, this is the first study to describe whether the recommendation for
 295 patients with stroke to spend at least 90% of their admission in a SU is a relevant indicator of
 296 high quality stroke care. We demonstrated an association between patients who spent at least
 297 90% of their admission in a SU and a reduced LOS, fewer severe complications and less
 298 discharges to a residential aged care facility. Similar results were evident from the primary
 299 analyses using the whole sample and propensity score matching, leading to more confidence
 300 in the validity of results. While results are based on stroke care provided in Australian
 301 hospitals, these findings are important for promoting and ensuring that patients with stroke
 302 spend most of their acute hospital stay in a SU and can be generalised to other countries with
 303 similar models of stroke care.

304 Although researchers have established that management of patients in a SU is
 305 associated with a reduction in length of hospital stay compared to other wards,^{21, 22} our
 306 findings have further demonstrated that length of time spent in a SU may also be important.

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3 307 Given the demands for beds in SUs,²² the two day reduction in LOS observed in our study is
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5 308 clinically important. Additionally, from an economic perspective, this reduction in LOS
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7 309 translates to potentially large cost-savings.²³ We acknowledge that given the study design we
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9 310 cannot make inferences about causality. Clinically, a longer LOS may be a consequence of
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11 311 experiencing a severe complication (as by definition may increase time in hospital), a more
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13 312 severe form of stroke, or delays in access to the next stage of care. Although more patients
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15 313 with a severe complication were not treated in a SU, for those who did access SU care and
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17 314 experienced a severe complication, there was no difference in LOS based on the proportion
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19 315 of time spent in the SU. The reduced likelihood of discharge to residential aged care facility
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21 316 for those spending >90% of time in the SU is potentially resultant from transfers to other
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23 317 wards when waiting for longer-term care. Regardless, with the additional trend towards
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25 318 reduced mortality for patients who spent at least 90% of admission in a SU, these results lend
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27 319 further support for ensuring that all patients with stroke spend most of their acute admission
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29 320 in a SU.
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33 321 Given that spending at least 90% of admission in a SU potentially influences
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35 322 outcomes, we have further demonstrated factors that are responsible for achieving this
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37 323 indicator. The main finding is that being admitted to a SU within three hours of arrival to the
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39 324 ED was independently associated with spending at least 90% of admission in a SU. This
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41 325 finding is of great importance because early admission to a SU has also been associated with
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43 326 better recovery.²⁴ Given evidence that SU care significantly reduces death and disability after
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45 327 stroke,^{3,4} and that the clinical guidelines for management of stroke recommend direct or early
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47 328 admission to a SU,⁵ our finding provides further evidence that early admission on a SU
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49 329 should be a high priority for clinicians and health administrators. While direct access to
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51 330 computed tomography from ambulance arrival has been achieved in some hospitals with the
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53 331 introduction of 'Code Stroke',²⁵ consideration of the added benefits for patients of direct
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3 332 admissions to stroke units is warranted. Unfortunately, overall access to SU in different
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5 333 countries remains highly variable. For example, in Australia only 67% of the patients with
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7 334 stroke received SU care in 2015.¹² This is a major difference to countries like the United
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9 335 Kingdom where 96% of patients received SU care.¹³ There is need to improve access as well
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11 336 as timely admission to a SU.

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13 337 Additionally, having a brain scan within 24 hours of arrival to the ED was associated
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15 338 with spending at least 90% of admission in a SU. An early brain scan is important for
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17 339 confirming the type of stroke and to exclude stroke mimics, thus enabling commencement of
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19 340 time-dependent therapies.⁵ The fact that patients who spent at least 90% of their admission in
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21 341 a SU were more likely to begin rehabilitation therapy within 48 hours of initial assessment
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23 342 highlights the importance of this indicator. These findings provide impetus for early
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25 343 assessment and early admission of all stroke patients onto a SU as this may help to advocate
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27 344 for patients to spend most of their acute hospital stay in a SU.

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29 345 Having at least 10 beds on the SU was associated with spending at least 90% of
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31 346 admission in a SU and this finding provides a strong argument for capacity building and
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33 347 potential redistribution of resources within hospitals to better support care for patients with
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35 348 stroke where there is the relevant throughput of patients.¹²

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37 349 There are some limitations that must be acknowledged. The time for discharge from
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39 350 the SU and hospital was unavailable. Therefore, our analysis was limited to dates which do
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41 351 not provide fine granularity that time would have provided. Also some observations were
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43 352 excluded because of invalid or missing dates. The comprehensive dataset did allow us to
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45 353 adjust our multivariable models for a number of comorbidities and patient variables,
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47 354 including stroke severity, for which we used a validated prognostic model. However, we
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49 355 acknowledge that the influence of unmeasured confounders such as socioeconomic status,
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51 356 and other comorbidities could not be fully addressed. Data on patients' ward of first
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3 357 admission, or transfers during the admission were not collected which precludes us from
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5 358 making definitive conclusions such as whether individuals with severe stroke or who suffer
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7 359 severe complications are admitted or transferred to the intensive care unit or other high
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9 360 dependency units first before admission on a SU or during their acute stay. Although there is
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11 361 evidence that SU care reduces mortality through prevention and treatment of infection and
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13 362 immobility-related complications,²⁶ having these additional data would have provided
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15 363 insight to why patients with severe stroke or severe complications were less likely to spend at
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17 364 least 90% of their admission in a SU. Additional longer-term outcomes would also be
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19 365 beneficial. Given these limitations and the nature of the study design which precludes us from
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21 366 drawing firm conclusions about temporal relationships, these findings should be interpreted
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23 367 with caution. The above limitations notwithstanding, a strength of our study is the large data
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25 368 set from a wide cross-section of Australian hospitals which provides national representation.
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369 **Conclusions**

370 Spending at least 90% of time in a SU is a useful measure of care quality and was
371 associated with better patient outcomes such as shorter LOS, fewer severe complications and
372 less discharge to aged care facilities. Our findings have important implications for clinical
373 practice and development of new models of stroke care.
374

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381 **Disclosures**

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390 **Authors and individual contributions**

391 DB, MK, DC were responsible for study concept and design. DB, TP, JK, MK were
392 responsible for statistical analyses. DB drafted the manuscript. DB, MK, TP, JK, SM, BC,
393 DC interpreted the data, critically revised the manuscript for important intellectual context
394 and approved the final version for submission. DB, MK, TP, JK, SM, BC, DC agree to be
395 accountable for all aspects of the work.

396 **Data Sharing Statement**

397 Contact can be made with the corresponding author for queries relating to
398 unpublished data.

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3 **476 Figure Legend**
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6 **477 Figure 1. Differences in complications between patients who spent at least 90% and**
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8 **478 those who spent less than 90% of their admission in a stroke unit.**

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11 **479 *significant $p < 0.05$; ^asymptomatic haemorrhagic transformation.**
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21 **482 Supplemental information**
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23 483 Supplemental Table A: Characteristics of patients with stroke treated in a stroke unit versus
24 484 those not treated in a stroke unit

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27 485 Supplemental Table B. Characteristics of patients with stroke who spent at least 90% and
28 486 those who spent less than 90% of admission in a stroke unit

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31 487 Supplemental Table C. Adherence to processes of care for patients who spent at least 90%
32 488 and those who spent less than 90% of hospital stay in a stroke unit

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35 489 Supplemental Methods for Propensity score matching with stratification

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37 490 Supplemental Table D. Adjusted beta coefficient for differences between treatment groups
38 491 (Model A)

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41 492 Supplemental Table E: Adjusted beta coefficient for differences between treatment groups
42 493 (Model B)

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45 494 Supplemental Table F. Association between percentages of hospital stay spent in a stroke unit
46 495 and in-hospital outcomes of patients with stroke

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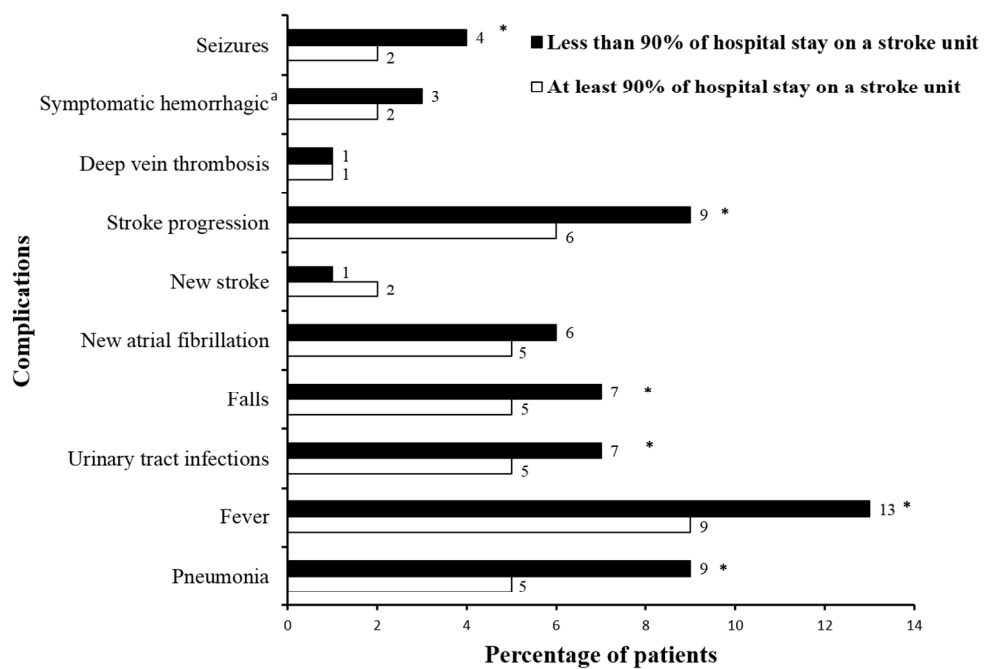


Figure 1. Differences in complications between patients who spent at least 90% and those who spent less than 90% of their admission in a stroke unit

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3 **Is length of time in a stroke unit associated with better outcomes for patients with stroke in**
4 **Australia? An observational study**
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Supplemental Table A. Characteristics of patients with stroke treated in a stroke unit versus those not treated in a stroke unit

Treated in a stroke unit	Yes (N= 2739) n (%)	No (N=684) n (%)	p-value
Patient characteristics			
Age, median (Q1, Q3)	76 (65, 84)	77 (65, 86)	0.03
Male	1530 (56)	347 (51)	0.02
Living at home prior to stroke	2522 (92)	586 (86)	<0.001
Independent prior to stroke (mRS 0–2)	2280 (83)	496 (73)	<0.001
In hospital stroke	75 (3)	54 (8)	<0.001
Stroke type			
Ischaemic stroke	2302 (84)	449 (66)	<0.001
Haemorrhagic stroke	286 (10)	163 (24)	<0.001
Unknown stroke type	151 (6)	72 (11)	<0.001
Stroke severity			
Arm weakness on admission	1675 (62)	352 (59)	0.18
Impaired speech on admission	1582 (59)	333 (57)	0.43
Unable to walk on admission	1454 (54)	392 (59)	0.02
Incontinence at 72 hours of admission	857 (32)	258 (42)	<0.001
History of comorbidities			
Atrial fibrillation			
Hypercholesterolemia	1058 (44)	225 (43)	0.73
Hypertension	1820 (70)	419 (70)	0.92
Diabetes mellitus	669 (27)	160 (29)	0.36
Ischaemic heart disease	670 (28)	175 (33)	0.02
Previous stroke or TIA	814 (33)	221 (39)	0.007
Organisational characteristics			
Metropolitan hospital	2672 (98)	661 (97)	0.18
Private hospital	217 (8)	37 (5)	0.03
Stroke care coordinator present	1626 (59)	446 (65)	0.005
Access to onsite neurosurgery	1000 (37)	210 (31)	0.004
Dedicated multi-disciplinary team present	2706 (99)	677 (99)	0.69
ED protocols for rapid triage	2625 (96)	643 (94)	0.04
Access to on site MRI within 24 hours	2136 (78)	517 (76)	0.18
Stroke team involved in quality improvement in last 2 years	2416 (88)	543 (79)	<0.001
Clinical care pathways for managing stroke present	2339 (85)	569 (83)	0.15
Access to early supported discharge team	338 (12)	103 (15)	0.06
Patients given discharge care plan	1275 (47)	347 (51)	0.05
Regular multi-disciplinary team meetings	2683 (98)	665 (97)	0.24
Arrangements with ambulance for rapid transfers	1897 (73)	498 (78)	0.003

Treated in a stroke unit	Yes (N= 2739) n (%)	No (N=684) n (%)	p-value
Offering thrombolysis	2404 (88)	606 (89)	0.55
Program for continuing education of staff	2609 (95)	649 (95)	0.69
Number of beds on SU			<0.001
<5	1246 (45)	380 (56)	
5-9	790 (29)	179 (26)	
≥10	703 (26)	125 (18)	
Stroke admissions last year ≥100	2558 (93)	602 (88)	<0.001
CT scanning within 3 hours for all patients	2690 (98)	676 (99)	0.26
Clinical processes of care			
Brain scan within 24 hrs of ED arrival	2108 (96)	496 (96)	0.35
Assessment in the ED	1071 (44)	127 (28)	<0.001
Time-critical therapy			
Thrombolysis in ischaemic stroke (with exclusions)	198 (10)	24 (6)	0.01
Assessment for rehabilitation by a physiotherapist within 24-48 hours of hospital admission	1605 (59)	198 (29)	<0.001
Rehabilitation therapy within 48 hours of initial assessment	1899 (89)	249 (67)	<0.001
Transition from hospital care			
Written care plan	1113 (61)	192 (48)	<0.001
Outcomes			
Any severe complication ^a	277 (10)	135 (20)	<0.001
Independent on discharge (mRS 0-2)	1285 (51)	263 (51)	0.84
Died in hospital	207 (8)	170 (25)	<0.001
Discharge destination (survivors)			
Private residence	1350 (53)	293 (57)	0.13
Residential aged care facility	156 (6)	43 (8)	0.07
Inpatient rehabilitation	785 (31)	77 (15)	<0.001
Other hospital ward	191 (8)	90 (18)	<0.001
In-hospital complications			
Aspiration Pneumonia	183 (7)	45 (7)	0.92
Falls	167 (6)	26 (4)	0.02
Fever	289 (11)	75 (11)	0.75
Urinary tract infections	169 (6)	30 (4)	0.07
New stroke	47 (2)	38 (6)	<0.001
Stroke progression	187 (7)	82 (12)	<0.001
New onset atrial fibrillation	155 (6)	28 (4)	0.10
Symptomatic haemorrhagic transformation	73 (3)	26 (4)	0.11
Deep vein thrombosis	15 (1)	4 (1)	0.91
Seizures	67 (2)	34 (5)	<0.001

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3 Q1: 1st quartile; Q3: 3rd quartile; ED: emergency department; SU: stroke unit; mRS: modified
4 Rankin scale. TIA: transient ischaemic attack; MRI: magnetic resonance imaging; ^aa
5 complication considered incapacitating, life threatening and one that prolongs hospital admission
6 and patient acuity including pneumonia, falls, fever, urinary tract infection, seizures, deep vein
7 thrombosis etc.
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Supplemental Table B. Characteristics of patients with stroke who spent at least 90% and those who spent less than 90% of admission in a stroke unit

Spent at least 90% of admission in a stroke unit	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Patient characteristics			
Living at home prior to stroke	1543 (91)	898 (93)	0.24
Arrived by ambulance ^a	1145 (76)	678 (79)	0.21
History of comorbidities			
Hypercholesterolemia ^a	653 (44)	366 (43)	0.69
Hypertension ^b	1123 (70)	644 (71)	0.76
Diabetes mellitus ^c	401 (26)	253 (29)	0.14
Previous stroke or TIA ^c	513 (34)	277 (32)	0.49
Clinical processes of care			
Brain scan within 3 hrs of ED arrival ^d	1053 (77)	567 (75)	0.24
Organisational characteristics			
Dedicated multi-disciplinary team present	1669 (99)	953 (98)	0.28
ED protocols for rapid triage	1626 (96)	919 (95)	0.07
Access to on site MRI within 24 hours	1306 (77)	765 (79)	0.33
Clinical care pathways for managing stroke present	1452 (86)	827 (85)	0.65
Patients given discharge care plan	772 (46)	464 (48)	0.28
Arrangements with ambulance for rapid transfers	1163 (73)	675 (73)	0.90
Offering thrombolysis	1490 (88)	838 (87)	0.19
Standardised processes to assess rehabilitation	1346 (80)	749 (77)	0.14
Program for continuing education of staff	1603 (95)	926 (96)	0.46
Neurologist involved in stroke management	1224 (73)	720 (74)	0.31
CT scanning within 3 hours for all patients	1651 (98)	955 (99)	0.15

ED: emergency department; TIA: transient ischaemic attack; CT: computed tomography; ^a11-15% unknown/not documented data; ^b1-5% unknown/not documented data; ^c6-10% unknown/not documented data; ^d16-20% unknown/not documented data.

Supplemental Table C. Adherence to processes of care for patients who spent at least 90% and those who spent less than 90% of hospital stay in a stroke unit

Spent at least 90% of hospital stay in a stroke unit	Yes (N= 1687) n (%)	No (N=968) n (%)	p-value
Early assessment			
Assessment in the ED	675 (44)	367 (43)	0.79
Time-critical therapy			
Transport by ambulance to hospital able to provide thrombolysis	1015 (76)	597 (79)	0.23
Thrombolysis in ischaemic stroke (with exclusions) ^a	99 (8)	94 (13)	<0.001
Thrombolysis in ischaemic stroke for those who arrive within 4.5 hours of symptom onset	88 (25)	83 (36)	0.003
Thrombolysis within 60 minutes of hospital arrival	32 (32)	20 (21)	0.08
Time (median) from onset of symptoms to thrombolysis (Q1,Q3)	2.8 (1.9, 3.7)	3 (2.3, 3.8)	0.10
Early rehabilitation			
Assessment for rehabilitation by a physiotherapist within 24-48 hours of hospital admission ^b	1185 (70)	643 (66)	0.04
Rehabilitation therapy within 48 hours of initial assessment	1161 (90)	673 (86)	0.01
Treatment for a rehabilitation goal commencing during an acute hospital admission	1256 (94)	738 (92)	0.14
Minimising risk of another stroke			
Discharge on antihypertensive medication ^c	701 (75)	404 (77)	0.54
Discharge on statin, antihypertensive and antithrombotic medications (ischaemic stroke) ^d	526 (66)	285 (66)	0.84
Discharge on oral anticoagulants for atrial fibrillation (ischaemic stroke)	144 (68)	87 (63)	0.38
Risk factor modification advice before leaving hospital	597 (61)	353 (64)	0.32
Carer training and support			
Carer support needs assessment	113 (64)	79 (72)	0.13
Carer training	99 (55)	58 (56)	0.87
Transition from hospital care			
Written care plan	699 (62)	377 (59)	0.16

ED: emergency department; Q1: 1st quartile; Q3: 3rd quartile; SU: stroke unit; ^a patients with pre-morbid functional impairment, recent surgery, major comorbidity, warfarin with INR>1.7, rapidly improving, imaging showing spontaneous reperfusion, other contraindication; ^b recorded as within 48 hours; ^c excludes those contraindicated to treatment; ^d excludes those where treatment was contraindicated or futile, or the patient refused.

Supplemental Methods

Propensity score matching with stratification

Since length of stay (LOS) in a stroke unit can be affected by clinical factors and bed availability, propensity score matching was used to minimise confounding by indication. Group comparisons were made within subgroups of patients with similar propensity scores.

A propensity score indicating the probability of being treated on a stroke unit for $\geq 90\%$ was generated for each participant based on a multivariable logistic regression model. Clinical characteristic variables that were associated with being treated on a stroke unit for $\geq 90\%$ in the univariable analysis were included in the multivariable logistic regression model. Being transferred to the stroke unit within 3 hours of arrival to the emergency department was included as a marker for bed availability at the time of admission. Severe complications were also included in the model where relevant since this is a marker for clinical characteristics as well as an outcome.

After the propensity scores were generated, patients were stratified into 5 quintiles of the propensity score. Group comparisons were conducted within the 5 quintiles of the propensity score, and overall with quintiles of the propensity score with the poorest matching of variables included in the multivariable logistic regression model used to generate the propensity score. Multivariable logistic regression was conducted for the analysis of binary outcomes with median regression modelling with bootstrap estimated standard errors for LOS. All analyses were adjusted for the propensity score quintile and clustering by hospital.

Propensity score generated including severe complications as a variable in the multivariable logistic regression model (Model A)

A propensity score was generated for 734 patients who spent $< 90\%$ of their admission in a stroke unit and 1372 patients who spent $\geq 90\%$ of their admission in a stroke unit.

Numbers of patients within the quintiles of the propensity score (Model A)		
	<90% time spent in a stroke unit	$\geq 90\%$ time spent in a stroke unit
Propensity score quintiles	N	N
1	185	237
2	170	251
3	147	274
4	143	278
5	89	332
Total	734	1372

Several differences in the characteristics of patients were apparent between the treatment groups within the quintiles of the propensity score.

Within quintile 1, there were differences between treatment groups in the proportion of patients who were unable to walk on admission ($p=0.046$) and suffered a severe complication while in hospital ($p=0.013$).

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3 Within quintile 4, there was a difference between treatment groups in the proportion of patients
4 who had a previous history of ischaemic heart disease (p=0.007).
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6 Within quintile 5, there were difference between treatment groups in the proportion of patients
7 who had impaired speech on admission (p=0.021) and were transferred to the stroke unit within 3
8 hours of arrival to the emergency department (p=0.041).
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10 In quintiles 1, 2 and 3, all patients were not transferred to the stroke unit within 3 hours of arrival
11 to the emergency department. In quintiles 2 and 3, there were no patients who experienced severe
12 complications.
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16 **Differences in characteristics between treatment groups within quintiles (Model A)**

	p-values for differences in characteristics between treatment groups within quintiles				
	1	2	3	4	5
Age	0.524	0.366	0.850	0.309	0.884
Intracerebral Haemorrhage	0.765	0.989	0.391	0.831	0.665
Arm weakness on admission	0.980	0.890	0.366	0.992	0.139
Impaired speech on admission	0.432	0.943	0.650	0.213	0.021
Unable to walk on admission	0.046	0.430	0.429	0.253	0.610
Incontinence at 72 hours of admission	0.842	0.708	0.747	0.334	0.649
Atrial fibrillation	0.281	0.274	0.899	0.812	0.565
Ischaemic heart disease	0.186	0.693	0.927	0.007	0.611
Transferred to SU within 3 hours of ED arrival	-	-	-	0.704	0.041
Severe complication	0.013	-	-	0.704	0.051

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37 There were no differences between treatment groups within quintiles of the propensity score
38 where there was good matching of characteristics between treatment groups (Table D). Death was
39 predicted perfectly in the model within quintile 4.
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42 **Table D. Adjusted beta coefficient for differences between treatment groups (Model A)**

Quintile	β coefficient (95% confidence interval), p-value reference category: <90% time spent in a stroke unit		
	Death	Discharged to residential aged care	Length of stay (discharged patients)
1	-0.48 (-0.93, -0.04), 0.03	-0.63 (-1.26, -0.01), 0.047	-5.0 (-9.49, -0.51), 0.03
2	-0.41 (-1.50, 0.69), 0.47	0.03 (-0.83, 0.88), 0.95	-2.0 (-3.60, -0.40), 0.01
3	-0.63 (-3.43, 2.17), 0.66	-0.51 (-1.46, 0.43), 0.29	-3.0 9-4.41, -1.60), <0.001
4	-	-1.59 (-2.99, -0.20), 0.025	-1.0 (-2.00, 0.003), 0.051
5	-0.66 (-1.52, 0.30), 0.18	-1.98 (-3.40, -0.57), 0.006	-3.0 (-4.34, -1.67), <0.001
2 and 3	-0.43 (-1.46, 0.60), 0.411	-0.15 (-0.81, 0.51), 0.662	-2.0 (-2.99, -1.01), <0.001
Overall	-0.43 (-0.82, -0.05), 0.026	-0.62 (-1.07, -0.16), 0.008	-3.0 (-4.01, -1.99), <0.001

Propensity score generated excluding severe complications as a variable in the multivariable logistic regression model (Model B)

A propensity score was generated for 746 patients who spent <90% of their admission in a stroke unit and 1387 patients who spent \geq 90% of their admission in a stroke unit.

Numbers of patients within the quintiles of the propensity score (Model B)		
	<90% time spent in a stroke unit	\geq 90% time spent in a stroke unit
Propensity score quintiles	N	N
1	186	241
2	169	258
3	148	278
4	147	280
5	96	330
Total	746	1387

There were fewer differences in the characteristics of patients apparent between the treatment groups within the quintiles of the propensity score when severe complications were not considered in the propensity score.

Within quintile 4, there were difference between treatment groups in the proportion of patients who had impaired speech on admission ($p=0.032$) and had a previous history of ischaemic heart disease ($p=0.011$).

Within quintile 5, there was a difference between treatment groups in the proportion of patients who were transferred to the stroke unit within 3 hours of arrival to the emergency department ($p=0.012$).

In quintiles 1, 2, 3 and 4 all patients were not transferred to the stroke unit within 3 hours of arrival to the emergency department.

Differences in characteristics between treatment groups within quintiles (Model B)					
	p-values for differences in characteristics between treatment groups within quintiles				
	1	2	3	4	5
Age	0.346	0.386	0.851	0.944	0.908
Intracerebral Haemorrhage	0.390	0.718	0.466	0.226	0.695
Arm weakness on admission	0.544	0.674	0.547	0.696	0.498
Impaired speech on admission	0.299	0.906	0.845	0.032	0.095
Unable to walk on admission	0.938	0.228	0.512	0.135	0.275
Incontinence at 72 hours of admission	0.552	0.555	0.765	0.468	0.811
Atrial fibrillation	0.536	0.349	0.945	0.912	0.675
Ischaemic heart disease	0.363	0.861	0.223	0.011	0.780
Transferred to SU within 3 hours of ED arrival	-	-	-	-	0.012

There were differences between treatment groups within quintiles of the propensity score where there was good matching of characteristics between treatment groups (Table E). There was a reduced chance of severe complications with greater time spent on a stroke unit within quintile 3 (p=0.013). When quintiles 1, 2 and 3 were aggregated, there was a reduced chance of severe complication (p=0.002) and death in hospital (p=0.039) with greater time spent on a stroke unit. Death was predicted perfectly in the model within quintile 4.

Table E. Adjusted beta coefficient for differences between treatment groups (Model B)

β coefficient (95% confidence interval), p-value				
reference category: <90% time spent in a stroke unit				
Quintile	Severe complication	Death	Discharged to residential aged care	Length of stay (discharged)
1	-0.41 (-0.86, 0.03), 0.069	-0.47 (-0.98, 0.04), 0.069	-0.49 (-1.06, 0.08), 0.091	-5.0 (-7.74, -2.26), <0.001
2	-0.36 (-1.07, 0.36), 0.328	-0.08 (-0.89, 0.73), 0.847	-0.17 (-0.96, 0.60), 0.664	-2.0 (-3.08, -0.92), <0.001
3	-1.14 (-2.04, -0.24), 0.013	-1.05 (-2.86, 0.76), 0.255	-0.67 (-1.64, 0.31), 0.183	-3.0 (-4.01, -1.99), <0.001
4	-0.10 (-1.33, 1.14), 0.877	-	-1.35 (-2.88, 0.18), 0.083	-1.0 (-1.87, -0.13), 0.025
5	-0.89 (-1.52, -0.15), 0.018	-0.57 (-1.51, 0.36), 0.228	-1.73 (-3.22, -0.24), 0.023	-3.0 (-4.15, -1.85), <0.001
1, 2 and 3	-0.49 (-0.81, -0.18), 0.002	-0.40 (-0.77, -0.02), 0.039	-0.42 (-0.86, 0.02), 0.058	-3.0 (-3.77, -2.22), <0.001
Overall	-0.52 (-0.81, -0.23), 0.001	-0.41 (-0.77, -0.05), 0.026	-0.59 (-1.02, -0.15), 0.008	-3.0 (-3.80, -2.20), <0.001

Interpretation of propensity score matching analyses

There is some evidence of benefit from a greater proportion of time spent in a stroke unit when confounding by indication is controlled

Supplemental Table F. Association between percentages of hospital stay spent in a stroke unit and in-hospital outcomes of patients with stroke

Model	Percentage of time spent in a SU (%)	aOR ^a	95% CI	P-value
1	Any severe Complications ^b			
	< 50	1		
	≥50 to <60	1.35	(0.68, 2.69)	0.40
	≥60 to <70	0.56	(0.23, 1.36)	0.20
	≥70 to <80	0.54	(0.23, 1.26)	0.15
	≥80 to <90	0.51	(0.25, 1.05)	0.07
	≥90	0.47	(0.30, 0.74)	0.001
2	LOS less than or equal to median LOS (5 days) - discharged			
	< 50	1		
	≥50 to <60	7.31	(4.12, 12.97)	<0.001
	≥60 to <70	9.15	(5.14, 16.27)	<0.001
	≥70 to <80	6.31	(3.52, 11.31)	<0.001
	≥80 to <90	2.27	(1.28, 4.02)	0.005
	≥90	9.71	(6.42, 14.69)	<0.001
3	Independent at discharge (mRS 0-2)			
	< 50	1		
	≥50 to <60	1.67	(0.90, 3.10)	0.10
	≥60 to <70	1.61	(0.89, 2.91)	0.11
	≥70 to <80	2.02	(1.08, 3.79)	0.03
	≥80 to <90	1.07	(0.60, 1.90)	0.82
	≥90	1.57	(1.07, 2.28)	0.02

SU: stroke unit; aOR: adjusted odds ratio; CI: confidence interval; LOS: length of stay; mRS: modified Rankin scale. ^aModels adjusted for age, gender, premorbid function, stroke type, stroke severity and past history of atrial fibrillation. ^ba complication considered incapacitating, life threatening and one that prolongs hospital admission and patient acuity including pneumonia, falls, fever, urinary tract infection, seizures, deep vein thrombosis etc.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found (Page 2)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (Page 4)
Objectives	3	State specific objectives, including any prespecified hypotheses (Page 4)
Methods		
Study design	4	Present key elements of study design early in the paper (Page 5)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (Page 5 & 6)
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants (Page 6)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (Page 6 & 7)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (Page 6 & 7)
Bias	9	Describe any efforts to address potential sources of bias (Page 7 & 8)
Study size	10	Explain how the study size was arrived at (Page 5)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (Page 6 & 7)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (Page 7 & 8) (b) Describe any methods used to examine subgroups and interactions (Page 7 & 8) (c) Explain how missing data were addressed (Page 6 & 7) (d) If applicable, describe analytical methods taking account of sampling strategy (N/A) (e) Describe any sensitivity analyses (Page 8)
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (Page 9) (b) Give reasons for non-participation at each stage (N/A) (c) Consider use of a flow diagram (N/A)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (Page 9, Table 1) (b) Indicate number of participants with missing data for each variable of interest (Table 1)
Outcome data	15*	Report numbers of outcome events or summary measures (Page 12, 13, Table 2, Table 3)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (Page 12, Page 13, Page 14, Table 2,

Table 3)

		(b) Report category boundaries when continuous variables were categorized (N/A)
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period (N/A)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses (Page 13, Supplemental Table D, E, F)
Discussion		
Key results	18	Summarise key results with reference to study objectives (Page 16)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (Page 17 & 19)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (Page 17, Page 19)
Generalisability	21	Discuss the generalisability (external validity) of the study results (Page 17)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (Page 20)

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.