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Vital sign monitoring following stroke associated with 90-day independence: A secondary analysis of the QASC cluster randomized trial

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ABSTRACT

Background: The Quality in Acute Stroke Care Trial implemented nurse-initiated protocols to manage fever, hyperglycaemia and swallowing (Fever, Sugar, Swallow clinical protocols) achieving a 16% absolute improvement in death and dependency 90-day post-stroke.
Objective: To examine associations between 90-day death and dependency, and monitoring and treatment processes of in-hospital nursing stroke care targeted in the trial.
Design: Secondary data analysis from a single-blind cluster randomised control trial.
Setting: 19 acute stroke units in New South Wales, Australia.
Participants: English-speakers ≥18 years with ischaemic stroke or intracerebral haemorrhage arriving at participating stroke units <48 h of stroke onset, excluding those for palliation and without a telephone.
Method: Data from patients in the 10 intervention hospitals and the nine control hospitals in the QASC trial post-intervention cohort, who had both hospital process of care data and 90-day outcome data were included. Associations between independence at 90-day (modified Rankin Score ≤1) and processes of care for fever, hyperglycaemia, and dysphagia screening were examined using multiple logistic regression adjusting for treatment group, sex, age group, premorbid modified Rankin scale, marital status, education, stroke severity and correlation within hospitals.
Results: Of 1126 patients in the post-intervention cohort (intervention or control), 970 had both in-hospital processes of care data and 90-day outcome data. Patients had significantly lower odds of 90-day independence if, within the first 72 h of stroke unit admission, they had one or more: febrile event (≥37.5 °C) (OR 0.47; 95%CI:0.35-0.61; P < 0.0001), higher mean temperature (OR:0.25; 95%CI:0.14-0.45; P < 0.0001), finger-prick blood glucose reading ≥11 mmol/L (OR:0.61; 95%CI:0.47-0.79; P = 0.0002), higher mean blood glucose (OR 0.89; 95%CI:0.84-0.95; P = 0.0006), or failed the swallowing screen (OR 0.35; 95%CI:0.22-0.56; P < 0.0001). Patients had greater odds of independence when: venous blood

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glucose was taken on admission to hospital or within 2 h of stroke unit admission (OR 1.4; 95%CI:1.01–1.83; P = 0.04); finger-prick blood glucose was measured within 72 h of stroke unit admission (OR 1.3; 95% CI:1.02-1.55; P = 0.03); or when swallowing screening or assessment was performed within 24 h of stroke unit admission (OR 1.8; 95%CI:1.29-2.55; P = 0.0006).
Conclusion: We have provided robust evidence of the importance of monitoring patients' temperature, blood glucose and swallowing status to improve 90-day stroke outcomes. Routine nursing care can result in significant reduction in death and dependency post-stroke.

What is already known about the topic?

- Fever, hyperglycaemia and swallowing difficulties post-stroke are significant problems resulting in increased morbidity and mortality.
- We demonstrated a 15.7% reduction in death and dependency following facilitated implementation of three nurse-initiated clinical protocols to manage fever, hyperglycaemia and swallowing difficulties in our previously published Quality in Acute Stroke Care (QASC) cluster randomised trial.

What this paper adds

- This novel secondary analysis of data from the QASC Trial provides further evidence for processes of stroke care that are associated with improved patient outcomes.
- Patients with stroke were more likely to be independent at 90 days when: venous blood glucose was taken on admission to hospital or within 2 h of stroke unit admission; finger-prick blood glucose was measured within 72 h of stroke unit admission; or when swallowing screening or assessment was performed within 24 h of stroke unit admission.
- Nurses adhering to protocols to manage fever, hyperglycaemia, and swallowing post-stroke demonstrate the importance of good surveillance.
- The exact mechanisms of how nursing care improves outcomes post-stroke remain unclear and could be a focus for future research.

1. Background

Fever, hyperglycaemia, and swallowing dysfunction are physiological variables known to be associated with poorer stroke outcomes (Capes et al., 2001; Greer et al., 2008; Martino et al., 2005; Williams et al., 2002). Elevation of temperature above 37.5 °C occurs in one third to one half of patients in the first days after stroke (National Stroke Foundation, 2015; Wang et al., 2000) and is associated with increased mortality, poor functional outcome and longer hospital stay (Greer et al., 2008). Post stroke hyperglycaemia occurs within 24 h in up to 68% of patients with stroke (Capes et al., 2001) and is associated with poor recovery (Capes et al., 2001; Williams et al., 2002) including increased infarct size (Pulsinelli et al., 1983) resulting in poorer outcomes independent of pre-stroke history of diabetes (Pulsinelli et al., 1983; Weir et al., 1997). Dysphagia is experienced by 42%–67% of patients within three days of stroke onset (Martino et al., 2005) and patients with dysphagia are three times more likely to develop pneumonia (Hinchey et al., 2005; Martino et al., 2005). Optimal management of fever, hyperglycaemia and dysphagia have been identified in international guidelines as priorities for inpatient stroke management (European Stroke Organisation (ESO) Executive Committee and ESO Writing Committee, 2008; Intercollegiate Stroke Working Party, 2012; Jauch et al., 2013).

The Quality in Acute Stroke Care (QASC) cluster randomised controlled trial investigated the effect of an evidence-based implementation intervention to improve the management of fever, hyperglycaemia and swallowing (Middleton et al., 2011). We undertook a secondary analysis to identify which of the processes of care delivered as part of the QASC intervention were associated with greater patient level of independence post-stroke.

2. Methods

The participant recruitment methods, data collection and randomisation processes of the QASC trial previously have been published in full elsewhere (Drury et al., 2014a; Middleton et al., 2009,Middleton et al., 2011). In brief, our single-blind cluster randomised controlled trial randomised acute stroke units (clusters) to minimise contamination because our team building intervention was designed for implementation at the stroke unit level. Eligible stroke units were those located in large, tertiary referral hospitals across New South Wales, Australia, with immediate computed tomography access and on-site high dependency units. Stroke unit medical directors provided cluster guardian consent.

We prospectively recruited patients who spoke English, were 18 years of age or older, had a diagnosis of ischaemic stroke or intracerebral haemorrhage and arrived at a participating stroke unit within 48 h of stroke onset. Those who were for palliation only or who did not have a telephone were excluded. Two patient cohorts were recruited: a pre-intervention cohort (August 2005 to October 2007) to provide baseline data, and a post-intervention cohort (February 2008 to August 2010). All outcomes were assessed at the level of the patient. Patients consented to medical record access and to participation in a telephone survey 90-days following hospital admission.

Nineteen stroke units were stratified by their Australian National Stroke Unit Program designation - Category A or B (A had access to on-site neurosurgery vs B with no access) (Cadilhac et al., 2006) and by absolute numbers of pre-intervention patients provided per hospital (low [≤2 patients/month] or high [>2 patients/month] recruitment). An independent statistician with no connection to the trial undertook the randomisation using random number generating software. Allocation was concealed until provided to the Project Officer who assigned stroke units to groups. Blinded clinical research assistants recruited eligible consecutive patients. Patients were blinded to group allocation but clinicians delivering the intervention were not. All outcome assessors and the trial statistician were blinded to group allocation.

Intervention stroke units (n = 10) received clinical treatment protocols for the management of Fever, Sugar, Swallow alongside a multidisciplinary team building intervention consisting of two team-building workshops to identify barriers and enablers to the implementation of the protocols, two interactive outreach education visits and reminders in the form of site visits, telephone and e-mail support (Box Box 1). Control group stroke units (n = 9) received only an abridged copy of the existing national stroke management guidelines (Drury et al., 2014a; Middleton et al., 2011). The

Fever

1. Temperature monitored & charted 4 hourly for 72 hours following admission to acute stroke unit.
2. Temperature ≥37·5°C treated with paracetamol (IV intravenous , PR per rectum or oral), unless clinically contraindicated.

Sugar (Hyperglycaemia)

1. Formal glucose measured (venous blood not finger prick) on admission to hospital or admission to the acute stroke unit.
2. 1-6 hourly fingerprick blood glucose levels for 72 hours following admission depending on previous blood glucose level.
3. On admission, if blood glucose level between 8 and 16 commence saline infusion.
   If blood glucose level ≥ 11 and known diabetic, commence insulin.
   If blood glucose level ≥ 16 and not a diabetic, commence insulin.
4. If blood glucose level ≥ 11 at any time in first 72 hours following admission, commence insulin.

Swallowing

1. Nurses underwent dysphagia screening education program, which consisted of all nurses attending an in-service administered by the speech pathologist using a Digital Video Disk prepared specifically for this study.
2. Nurses underwent a competency assessment before being able to screen patients, consisting of an assessment of clinical knowledge tool, a written test and a clinical competency tool which had to be completed on three patients and was assessed by a Speech Pathologist.
3. Patients screened using the Screening of Swallowing in Stroke/ Transient Ischaemic Attack (ASSIST) dysphagia screening tool by either a nurse who passed the competency test or a Speech Pathologist within 24 hours of admission to the acute stroke unit; this then was clearly documented in the patient's medical record by use of a sticker.
4. Patients who failed the swallowing screening to be referred to a Speech Pathologist for a swallowing assessment.

Box 1. QASC Trial Fever, Sugar and Swallowing (FeSS) Clinical Protocols^.
^ The Fever, Sugar, Swallow clinical protocols, implementation strategy and Acute Screening of Swallowing in Stroke/ Transient Ischaemic Attack (ASSIST) dysphagia screening tool available at www.acu.edu.au/qasc.

Fever, Sugar, Swallow clinical protocols, the implementation strategy, the Acute Screening of Swallowing in Stroke/ Transient Ischaemic Attack (ASSIST) dysphagia screening tool are available at http://www.acu.edu.au/qasc.

Patients were followed up at 90-day post admission by outcome assessors blind to group allocation using a computer assisted telephone interview to examine 90-day survival and independence using the modified Rankin Scale (De Haan et al., 1995). Medical records of each participating patient were audited by independent research assistants blind to group allocation to examine five in-hospital processes of stroke care: temperature monitoring; fever management; glucose monitoring; hyperglycaemic management;

Fever

a) *Temperature readings 4 hourly for the first 72 hours of stroke unit admission* - met if a patient had at least five readings within each of the first three 24-hour periods following stroke unit admission.
b) *Paracetamol for temperature ≥ 37.5°C* - met if paracetamol administration (at the first febrile event) within 60 minutes of a temperature ≥ 37.5°C or already had received paracetamol within previous 5 hours.
c) *Treated according to Fever protocol* - met if patient met measure a) and either met measure b) or did not have a temperature reading ≥ 37.5°C

Sugar

a) *Venous blood glucose taken on hospital or stroke admission* - met if venous blood glucose taken in Emergency Department or within 2 hours of stroke unit admission.
b) *Finger-prick blood glucose measured on stroke unit admission* - met if finger-prick blood glucose measured in first 2 hours of stroke unit admission.
c) *Finger-prick blood glucose readings 6 hourly in the first 72 hours of stroke unit admission* - met if the patient had at least three finger-prick glucose measures within each of the first three 24-hour periods following stroke unit admission.
d) *Finger-prick blood glucose measured in first 72 hours of stroke unit admission* - met if patients had one or more glucose measured at any time during the first 72 hours of stroke unit admission
e) *Finger-prick blood glucose ≥11 mmol/L following stroke unit admission* - met if any glucose reading ≥11 mmol/L at any time during first 72 hours of stroke unit admission.
f) *Treated according to hyperglycaemia protocol* - of patients that met measure e, met if insulin administered within 2 hours of the relevent blood glucose reasing.
g) *Treated according to Sugar protocol* - met if patient met all of measures a), b), c) and where applicable, measure f).

Swallow

a) *Swallow screen in Emergency Department* - met if patients underwent a swallow screening in Emergency Department.
b) *Swallow screen in Emergency Department or within 24 hours of stroke admission* - met if patients underwent a swallowing screening in Emergency Department or within 24 hours of stroke unit admission.
c) *Swallow screen or assessment within 24 hours of stroke unit admission* - met if patients underwent a swallowing screening within 24 hours of stroke unit admission.
d) *Failed swallow screen* – met if patients that met measure b) failed the swallow screen.
e) *Seen by a speech pathologist* – met if patients that met measure d) were referred to a speech pathologist.
f) *Treated according to Swallow protocol* - met if patient met measure c) and where applicable, measure e).

Box 2. Acceptable practice measure definitions.

and dysphagia management. In addition, the following data also were collected: demographic data (age, sex, Aboriginal and Torres Strait Islander status, marital status, highest education qualification, employment status); clinical characteristics (pre-morbid modified Rankin Scale, stroke sub-type (Oxfordshire Community Stroke Project Classification) (Bamford and Sandercock, 1991), stroke severity (Llanes et al., 2004) (Los Angeles Motor Scale), time from symptom onset to presentation, intravenous tissue plasminogen activator administration; for the first 72 h following stroke unit admission: all temperature and blood glucose readings, administration of paracetamol, administration of saline, administration of insulin; swallowing screen and time, swallowing assessment and time, seen by speech pathologist for those who failed the swallow screen. For quality assurance, 10% of all records were re-audited.

Data were analysed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) by intention-to-treat. Data from patients in all the intervention hospitals (n = 10) and control hospitals (n = 9) in the post-intervention cohort of the QASC trial, who had both hospital process of care data and 90-day outcome data were included in this secondary analysis (Drury et al., 2014a; Middleton et al., 2011). The modified Rankin Scale was used as the outcome measure of dependency and dichotomised as ≤1 (independent) or ≥2 (dead or dependent). Mean temperature and finger-prick blood glucose levels were calculated for each patient for the first 72 h of admission to the stroke unit. A summary score was computed for treatment according to each of the fever, sugar and swallowing protocol elements. Definitions of variables are shown in Box Box 2.

Multiple logistic regression models were used to explore the association between independence and: temperature monitoring; fever management (treatment with paracetamol); finger-prick blood glucose monitoring; hyperglycaemic management; swallowing surveillance (screening and assessment). All analyses were adjusted for treatment group, sex, age group, premorbid modified Rankin Scale, marital status, education, stroke severity (Los Angeles Motor Scale) (0 = mild stroke; and >0 = severe stroke) and time from symptom onset to stroke unit presentation. Separate logistic regression models were fitted for each monitoring

Table 1
Association between baseline characteristics and 90-day independence.

Variable		Outcome		P value*
		Dead or Dependent (modified Rankin Scale ≥2) (n = 469) n (%)	Independent (modified Rankin Scale ≤1) (n = 501) n (%)	
Age group	Less than 65 years	123 (43%)	166 (57%)	<0.0001
	65 to 74 years	83 (34%)	163 (66%)	
	75 to 84 years	154 (53%)	138 (47%)	
	Over 85 years	109 (76%)	34 (24%)	
Sex	Male	273 (47%)	312 (53%)	0.1450
	Female	196 (51%)	189 (49%)	
Aboriginal or Torres Strait Islander	Yes	4 (36%)	7 (64%)	0.2732
	No	422 (46%)	493 (54%)	
Marital status	Never married	21 (35%)	39 (65%)	0.0018
	Married	253 (45%)	314 (55%)	
	Widowed/Divorced/Separated	153 (51%)	147 (49%)	
Highest education qualification	No school certificate	143 (54%)	122 (46%)	0.0058
	School certificate	159 (46%)	189 (54%)	
	Higher school certificate	59 (44%)	74 (56%)	
	University/Technical and Further Education/College	60 (34%)	114 (66%)	
Employment status	Retired	319 (51%)	307 (49%)	<0.0001
	Employed full time	12 (12%)	89 (88%)	
	Permanently unable to work or ill	78 (77%)	23 (23%)	
	Employed part-time or casual	6 (9.4%)	58 (91%)	
	Unemployed/Home duties/Volunteer work/Student	12 (34%)	23 (66%)	
Pre-morbid modified Rankin Scale	No symptoms at all	342 (41%)	486 (59%)	<0.0001
	No significant disability despite symptoms	27 (79%)	7 (21%)	
	Slight disability	32 (89%)	4 (11%)	
	Moderate disability	24 (89%)	3 (11%)	
	Moderately severe disability	3 (75%)	1 (25%)	
Oxfordshire Community Stroke Project Classification (S troke location)	Total Anterior Circulation Infarct	51 (91%)	5 (8.9%)	<0.0001
	Partial Anterior Circulation Infarct	175 (48%)	190 (52%)	
	Lacunar infarct	59 (39%)	91 (61%)	
	Posterior Circulation Infarct	60 (41%)	88 (59%)	
	Intracerebral Haemorrhage	21 (51%)	20 (49%)	
Los Angeles Motor Scale (stroke severity)	0 (mild)	124 (31%)	278 (69%)	<0.0001
	> 0 (severe)	338 (60%)	221 (40%)	
Time from symptom onset to stroke unit arrival (in hours)	< 3hrs	27 (48%)	29 (52%)	0.8977
	3 to < 6hrs	70 (53%)	61 (47%)	
	6 to < 12hrs	149 (50%)	147 (50%)	
	12 to < 24hrs	124 (45%)	149 (55%)	
	≥ 24hrs	99 (46%)	115 (54%)	
Thrombolysis	No	433 (48%)	468 (52%)	0.9777
	Yes	36 (52%)	33 (48%)	
Time from onset of symptoms to presentation (minutes)	mean (SD)	872.9 (683.5)#	914.4 (660.4)#	0.6017

*P-value from logistic model adjusting for correlation of patient outcomes within hospitals using General Estimating Equation approach.
mean (standard deviation [SD]).

and management process of care within a generalised estimating equation framework to adjust for the correlation of patient outcomes within hospitals. Post hoc power calculations estimated that there was 80% power, with 5% significance level, to detect differences in processes of care of 12%–15% for binary outcomes and 0.25 to 0.3 standard deviations for continuous outcomes, for design effects of 2 to 2.5 (based on intraclass correlation coefficients of 0.02-0.025 and allowing for varying cluster sizes).

3. Results

Of the 1126 patients from the 19 participating hospitals in the QASC post-intervention cohort (intervention and control group), 970 had both in-hospital processes of care audit data and 90-day outcome data (Supplementary Figure 1) (Middleton et al., 2011).

Over half the sample 501 (52%) were alive and independent at 90-day. Younger age, marital status (never married or married), higher education, being employed, independence pre- stroke (premorbid modified Rankin Scale ≤1), location of stroke (Oxfordshire Community Stroke Project Classification) and mild stroke severity (Los Angeles Motor Scale = 0) were associated with 90-day independence (Table 1).

Patients who experienced at least one febrile event (temperature ≥37.5 °C) within the first 72 h of stroke unit admission had a significantly lower odds of independence than patients without a febrile event (34% vs 57% respectively; OR 0.47, 95% CI:0.35-0.61; P < 0.0001) (Table 2). Further, higher mean temperature was associated with a lower odds of independence (OR 0.25; 95% CI:0.14-0.45; P < 0.0001). However, for patients who had a fever within 72 h of stroke unit admission, independence at 90-day was not associated with receipt of paracetamol or treatment according to the QASC Fever protocol.

Patients who had their venous blood glucose taken on admission to hospital or within 2 h of stroke unit admission (OR 1.4; 95%CI:1.01–1.83; P = 0.04) and those who had a finger-prick blood glucose level measured in the first 72 h post stroke (OR 1.3; 95% CI:1.02-1.6; P = 0.03) had a greater odds of independence at 90-day (Table 3). Higher mean finger-prick blood glucose in the first 72 h was associated with a significantly lower odds of independence (OR 0.89; 95% CI:0.84-0.95; P = 0.0006). Patients with a finger-prick blood glucose level reading ≥11 mmol/L during the first 72 h had lower odds of independence than patients without high blood glucose level (OR 0.61; 95% CI:0.47-0.79; P = 0.0002). In patients with elevated high blood glucose level, independence was not associated with treatment according to the QASC Sugar protocol. Of note, only 716 (74%) of patients had one or more finger-prick blood glucose measurements in first 72 h of stroke unit admission.

Patients had a greater odds of independence if they had a swallowing screen or swallowing assessment within 24 h of stroke unit admission (OR 1.8; 95% CI:1.3-2.6; P = 0.0006). Patients who were screened by a non-speech pathologist and who failed this screen had a lower odds of independence (OR 0.35; 95% CI:0.22-0.56; P < 0.0001) (Table 4).

4. Discussion

This secondary analysis of QASC trial data provide further important information on the processes of stroke care that were associated with improved patient outcomes. It also provides further evidence that adherence to the Fever, Sugar, Swallow protocols reduces death and dependency. Not unexpectedly, younger age, independence pre-stroke, mild stroke severity, full time employment, and stroke location were significantly associated with 90-day independence. However, of interest, being widowed, divorced or separated, and not having a school certificate (usually obtained at approximately 16 years of age) were associated with death or dependency.

We previously have reported associations between lower mean temperature and better outcomes (Drury et al., 2014a; Middleton et al., 2011) also supported by evidence from other studies (Hajat et al., 2000). Whilst statistically significant, the clinical importance of the 0.1°C difference is negligible. However, it remains unknown exactly what temperature level should trigger a point of clinical concern, and better yet, treatment. Many international stroke guidelines do not recommend an actual treatment point (United Kingdom, United States of America, Australia) (Intercollegiate Stroke Working Party, 2012; Jauch et al., 2013; National Stroke Foundation, 2010) whilst others recommend treatment at >37.5 °C (Europe, Canada) (Casaubon et al., 2015; European Stroke Organisation (ESO) Executive Committee and ESO Writing Committee, 2008). Our finding that temperature ≥37.5 °C

Table 2
Temperature monitoring and fever management practices associated with 90-day independence[§].

Variable		Outcome: Dead or dependent (modified Rankin Scale ≥2) (n = 469) n (%)	Outcome: Independent (modified Rankin Scale ≤1) (n = 501) n (%)	Odds Ratio (95% CI)	P-value[*]
Temperature readings 4 hourly for the first 72 h of stroke unit admission	No	333 (48%)	360 (52%)	1.00	0.6794
	Yes	136 (49%)	141 (51%)	0.93 (0.67–1.3)	
Temperature ≥37.5°C	No	325 (43%)	426 (57%)	1.00	<0.0001
	Yes	144 (66%)	75 (34%)	0.47 (0.35-0.61)	
Paracetamol given within 1 h (among those with temperature ≥37.5°C)	No	112 (66%)	58 (34%)	1.00	0.9547
	Yes	32 (65%)	17 (35%)	0.96 (0.28–3.33)	
Treated according to the Fever protocol	No	370 (49%)	380 (51%)	1.00	0.6744
	Yes	99 (45%)	121 (55%)	1.11 (0.69–1.78)	
Mean temperature reading - mean (SD)	mean (SD)	36.6 (0.3)[#]	36.5 (0.3)[#]	0.25 (0.14-0.45)[^]	<0.0001

[*] P-values from logistic model adjusting for treatment group, sex, age group, premorbid modified Rankin Scale, marital status, education, time to hospital, Los Angeles Motor Scale and correlation of patient outcomes within hospital using General Estimating Equation approach.
[#] mean (standard deviation [SD]).
[^] odds ratio associated with a 1° Celsius increase in temperature.
[§] variable definitions given in Box 2 .

Table 3
Glucose monitoring and hyperglycaemic management practices associated with 90-day independence[§].

Variable		Outcome			
		Dead or dependent (modified Rankin Scale ≥2) (n = 469) n (%)	Independent (modified Rankin Scale ≤1) (n = 501) n (%)	Odds Ratio (95% CI)	P-value[*]
Venous blood glucose taken on admission to hospital or within 2 h of stroke unit admission	No	380 (52%)	357 (48%)	1.00	0.0412
	Yes	89 (38%)	144 (62%)	1.36 (1.01–1.83)	
Finger-prick blood glucose measured in first 2 h of stroke unit admission	No	356 (50%)	361 (50%)	1.00	0.3508
	Yes	113 (45%)	140 (55%)	1.17 (0.84–1.63)	
Finger-prick blood glucose readings 6 hourly in the first 72 h of stroke unit admission	No	364 (48%)	396 (52%)	1.00	0.2779
	Yes	105 (50%)	105 (50%)	0.79 (0.52–1.21)	
Finger-prick blood glucose measured in first 72 h of stroke unit admission	No	135 (53%)	119 (47%)	1.00	0.0303
	Yes	334 (47%)	382 (53%)	1.26 (1.02–1.55)	
Finger-prick blood glucose ≥ 11 mmol/L following stroke unit admission	No	392 (47%)	440 (53%)	1.00	0.0002
	Yes	77 (56%)	61 (44%)	0.61 (0.47-0.79)	
Treated according to hyperglycaemia protocol (among those with finger-prick blood glucose ≥ 11 mmol/L)[$]	No	34 (52%)	31 (48%)	1.00	0.9407
	Yes	43 (59%)	30 (41%)	0.95 (0.43–2.11)	
Treated according to hyperglycaemia protocol[$]	No	460 (49%)	479 (51%)	1.00	0.0684
	Yes	9 (29%)	22 (71%)	1.77 (0.96–3.27)	
Mean finger-prick blood glucose in first 72 h of stroke unit admission – mean (SD)	mean (SD)	7.0 (1.9)[#]	6.7 (1.7)[#]	0.89 (0.84-0.95)[^]	0.0006

[*] P-values from logistic model adjusting for treatment group, sex, age group, premorbid modified Rankin Score, marital status, education, time to hospital, LAMS and correlation of patient outcomes within hospital using General Estimating Equation approach.
[#] mean (standard deviation [SD]).
[^] odds ratio associated with a 1 mmol/L increase in mean finger-prick blood glucose.
[$] adjusted for all factors above except premorbid modified Rankin Scale because model convergence problems.
[§] variable definitions given in Box 2 .

Table 4
Swallowing monitoring and management practices associated with 90-day independence[§].

Variable		Outcome			
		Dead or dependent (modified Rankin Scale ≥2) (n = 469) n (%)	Independent (modified Rankin Scale ≤1) (n = 501) n (%)	Odds Ratio (95% CI)	P-value[*]
Swallow screen in emergency department	No	358 (48%)	393 (52%)	1.00	0.6123
	Yes	111 (51%)	108 (49%)	1.08 (0.79–1.48)	
Swallow screen in emergency department or within 24 h of stroke unit admission	No	290 (52%)	272 (48%)	1.00	0.3957
	Yes	179 (44%)	229 (56%)	1.14 (0.84–1.55)	
Swallow screen or assessment within 24 h of stroke unit admission	No	47 (70%)	20 (30%)	1.00	0.0006
	Yes	422 (47%)	481 (53%)	1.81 (1.29–2.55)	
Failed swallow screen (among those screened in the emergency department or stroke unit)	No	109 (37%)	188 (63%)	1.00	<0.0001
	Yes	70 (63%)	41 (37%)	0.35 (0.22–0.56)	
Seen by a speech pathologist (among those who failed the swallow screen)	No	2 (40%)	3 (60%)	1.00	0.4414
	Yes	68 (64%)	38 (36%)	0.58 (0.15–2.29)	
Met all relevant swallow screen elements	No	292 (51%)	275 (49%)	1.00	0.4028
	Yes	177 (44%)	226 (56%)	1.14 (0.84–1.54)	

[*] P-values from logistic model adjusting for treatment group, sex, age group, premorbid modified Rankin Scale, marital status, education, time to hospital, Los Angeles Motor Scale and correlation of patient outcomes within hospital using General Estimating Equation approach.
[§] variable definitions given in Box Box 2.

was significantly associated with worse outcomes, provides evidence that a treatment trigger point of 37.5 °C could be beneficial, acknowledging the limited evidence to date for the effectiveness of antipyretics on patient outcomes (Den Hertog et al., 2009) and the lack of data to support an alternative temperature treatment trigger point. Providing clinicians with a clear temperature treatment trigger point may improve compliance with recommended treatments and improved patient outcomes.

Our results that treatment of fever with paracetamol within an hour was not significantly associated with improved outcomes may be due to the less than optimal overall compliance with this data element. Our previously published data showed that only 29% of control group and 21% of intervention group patients received paracetamol within two hours for their first febrile event (Drury et al., 2014a). However, we note that only n = 219 (23%) of our cohort were febrile requiring treatment. Despite this, many international stroke guidelines (European, United States of America, Canada and Australia) (Casaubon et al., 2015; Jauch et al., 2013; National Stroke Foundation, 2010; Ntaios et al., 2015) recommend treatment of fever with antipyretics as a good practice point.

Our data also support results from other studies demonstrating an association between lower mean blood glucose in the first 72 h with better 90-day outcomes (Yong and Kaste, 2008; Yoo et al., 2014). That only 716 (74%) of patients had one or more finger-prick blood glucose levels performed in the first 72 h of hospital

admission is less than optimal. Two of the glucose monitoring practices were associated with independence supporting routine glucose measurement (venous blood glucose taken on admission to hospital or within two hours of stroke unit admission; finger-prick blood glucose measured in first 72 h of stroke unit admission). However, treatment with saline or insulin for those with glucose ≥11 mmol/L were not associated with independence. While our trial aimed to control major episodes of hyperglycaemia (e.g. ≥11 mmol/L), other studies using insulin to tightly control glucose levels in acute stroke (e.g 4–7 mmol/L) also have shown no benefit (Gray et al., 2007).

Significant associations between 90-day independence and a swallow screen or assessment within 24 h of stroke unit admission, and failing a swallow screen supports the benefits of good swallowing surveillance. Nurse screening reduces pneumonia and length of stay (Palli et al., 2017), and delays in screening are associated with higher risk of pneumonia (Bray et al., 2017).

Collectively, data from our trial reinforce the importance of routine nursing practice to monitor and respond to fever, hyperglycaemia and swallowing management post-stroke (Drury et al., 2014a). Importantly, the primary aim of our trial was not to determine which component was more important, but the effect of bundled processes of care, all of which are recommended in international stroke clinical guidelines. This bundled approach aligns with international research supporting high quality stroke care processes and reduced 30-day mortality (Bray et al., 2013). In addition, in a recent study using data from the Australian Stroke Clinical Registry, researchers reported that adherence to three processes of care (stroke unit care, discharged with a care plan and discharged on anti-hypertensive medications) resulted in a 70% reduced hazard of death 180 days post-stroke and improved health-related quality of life, also supporting bundled care delivery ((Cadilhac et al., 2017)

It has been theorised that nursing surveillance (including monitoring) (Henneman et al., 2012) is a key causal pathway linking nursing practice to patient outcomes and that evidence about the impact of surveillance or missed care can guide management efforts to improve nursing care (Lake, 2014). However, the literature on vital sign monitoring provides little empirical evidence for prevailing regimes or recommended best practice (Storm-Versloot et al., 2014; Zeitz and McCutcheon, 2006) and further research is required. Our trial helps to fill this evidence gap by providing novel data linking vital sign monitoring by nurses with improved patient outcomes following stroke. Of note, adherence to the FeSS protocols was generally less than optimal ((Drury et al., 2014a). This was despite nurses from intervention stroke units assuring us prior to trial commencement that they already were managing these elements, which our baseline data showed clearly was not the case (Drury et al., 2014b). Hence, the precise mechanism for the improved outcome is not clear. As previously noted, by ourselves (Middleton, 2012) and others (Alberts, 2012), it is possible that the routine monitoring of our three physiological variables, fever, glucose and swallowing, revealed a deteriorating patient which may have triggered a medical review or other medical management, the measurement of which was beyond the scope of our trial. Nonetheless, our data support the findings of previous research outside stroke of the positive relationship between patient monitoring the resulting detection of physiological abnormalities and patient outcomes (Mitchell et al., 2010).

Our trial had methodological strengths. At the cluster level it was conducted in 19 of the 20 established New South Wales stroke units at the time, and at the patient level we achieved a large sample size. That our trial has included an analysis to determine associations between outcomes and processes of stroke care is laudable. Our deliberate exclusion of patients for palliation may have contributed to our mild to moderate cohort of stroke patients but we note that stroke severity was evenly distributed between groups.

Subsequent research from our team makes the clinical implications of this secondary analysis all the more noteworthy. In a recent study, we followed up patients in the QASC trial post-implementation cohort (n = 1076) and found that patients cared for in stroke units randomised to the intervention group were >20% less likely to die out to a median of 4.1 years post-stroke (Middleton et al., 2017). A recent independent economic analysis commissioned by the Australian Commission on Safety and Quality in Health Care has shown that if only 65% of all the eligible Australian population were to receive care in line with the Fever, Sugar, Swallow Protocols, there would be a $AUD281 M economic benefit (Australian Clinical Trials Alliance, 2017). Collectively, this sustained reduction in mortality along with a clear economic benefit provides further evidence for the effectiveness of the Fever, Sugar, Swallow clinical protocols. We have successfully implemented the Fever, Sugar, Swallow clinical protocols across all 36 New South Wales stroke services (Middleton et al., 2016) and now they are currently being implemented and evaluated in up to 12 countries in Europe (Mikulik et al., 2017). Arising from our research, the Australian 2017 Clinical Guidelines for Stroke Management now have a 'strong recommendation' that '*all acute stroke services should implement standardised protocols to manage fever, glucose and swallowing difficulties in stroke patients*' (Stroke Foundation, 2017).

These secondary analyses confirm the importance of nursing care for control of physiological variables unstable in the early critical phases of stroke. They provide valuable corroboration for clinicians of the importance of good nursing surveillance, which are generalizable internationally. By linking processes of care to patient outcomes this trial clearly demonstrates the importance and clinical value of good nursing care and routine vital sign monitoring.

Authorship

All authors meet the ICMJE recommended criteria for authorship. The following authors contributed significantly to the trial conception and design: SM, PM, CDE, DC, SD, JG, JW, CQ, NWC, CL. PD and SD assisted with data acquisition. SM, PM, CDE, SD, JW prepared the first draft of the manuscript. CDE and PM provided statistical expertise and conducted the primary statistical analyses. All authors revised the manuscript for important intellectual content and all authors approved the final manuscript for submission.

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Ethical approval

This study was approved by the National Human Research Ethics Committee of the Australian Catholic University and the relevant Human Research Ethics Committees at all participating hospitals.

Competing/Conflicting interests

The authors declare that they have no competing interests, or conflict of interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijnurstu.2018.09.014.

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