

Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): a cluster randomised controlled trial



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Summary

Background We assessed patient outcomes 90 days after hospital admission for stroke following a multidisciplinary intervention targeting evidence-based management of fever, hyperglycaemia, and swallowing dysfunction in acute stroke units (ASUs).

Methods In the Quality in Acute Stroke Care (QASC) study, a single-blind cluster randomised controlled trial, we randomised ASUs (clusters) in New South Wales, Australia, with immediate access to CT and on-site high dependency units, to intervention or control group. Patients were eligible if they spoke English, were aged 18 years or older, had had an ischaemic stroke or intracerebral haemorrhage, and presented within 48 h of onset of symptoms. Intervention ASUs received treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction with multidisciplinary team building workshops to address implementation barriers. Control ASUs received only an abridged version of existing guidelines. We recruited pre-intervention and post-intervention patient cohorts to compare 90-day death or dependency (modified Rankin scale [mRS] ≥ 2), functional dependency (Barthel index), and SF-36 physical and mental component summary scores. Research assistants, the statistician, and patients were masked to trial groups. All analyses were done by intention to treat. This trial is registered at the Australia New Zealand Clinical Trial Registry (ANZCTR), number ACTRN12608000563369.

Findings 19 ASUs were randomly assigned to intervention ($n=10$) or control ($n=9$). Of 6564 assessed for eligibility, 1696 patients' data were obtained (687 pre-intervention; 1009 post-intervention). Results showed that, irrespective of stroke severity, intervention ASU patients were significantly less likely to be dead or dependent (mRS ≥ 2) at 90 days than control ASU patients (236 [42%] of 558 patients in the intervention group vs 259 [58%] of 449 in the control group, $p=0.002$; number needed to treat 6.4; adjusted absolute difference 15.7% [95% CI 5.8–25.4]). They also had a better SF-36 mean physical component summary score (45.6 [SD 10.2] in the intervention group vs 42.5 [10.5] in the control group, $p=0.002$; adjusted absolute difference 3.4 [95% CI 1.2–5.5]) but no improvement was recorded in mortality (21 [4%] of 558 in intervention group and 24 [5%] of 451 in the control group, $p=0.36$), SF-36 mean mental component summary score (49.5 [10.9] in the intervention group vs 49.4 [10.6] in the control group, $p=0.69$) or functional dependency (Barthel Index ≥ 60 : 487 [92%] of 532 patients vs 380 [90%] of 423 patients; $p=0.44$).

Interpretation Implementation of multidisciplinary supported evidence-based protocols initiated by nurses for the management of fever, hyperglycaemia, and swallowing dysfunction delivers better patient outcomes after discharge from stroke units. Our findings show the possibility to augment stroke unit care.

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Introduction

Although organised stroke unit care significantly reduces death and disability from cerebrovascular events,¹ three physiological variables are not yet universally well managed despite their importance for long-term patient recovery.^{2–4} In the first days of an acute stroke, temperature higher than 37.5°C occurs in 20–50% of patients;² up to 50% become hyperglycaemic;³ and 37–78%⁴ have dysphagia; all result in increased morbidity and mortality.^{2–4} Hence, international guidelines recommend that fever and high blood glucose concentrations be monitored and managed proactively and that every stroke patient have their swallowing status evaluated before receiving food,

fluid, or oral medication.^{5,6} All these recommendations are the responsibility of the stroke multidisciplinary team.⁷ Care is not always consistent with these recommendations however.^{6,8} We designed the Quality in Acute Stroke Care (QASC) study, a cluster randomised controlled trial,^{9,10} to assess the effect of multidisciplinary team building workshops and a standardised interactive education programme to implement evidence-based treatment protocols for the management of fever, hyperglycaemia, and swallowing dysfunction on patient outcomes 90 days after admission for stroke. These three variables were selected because they implicate multidisciplinary teamwork, which has been shown to

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For the protocols and information about the intervention see <http://www.acu.edu.au/qasc>

improve health-care processes and patient outcomes,¹¹ a priority for stroke care.

Methods

Trial design and participants

Our single-blind cluster randomised controlled trial randomised Acute Stroke Units (ASUs) to minimise contamination because our team building intervention was designed for implementation at the ASU level.¹² Outcomes before and after intervention were assessed at the patient level. The trial protocol has been published previously.⁹ All treatment protocols, the ASSIST dysphagia screening tool, and further information about implementation of the intervention are available at the Australian Catholic University website.

ASUs eligible to participate were those located in large, tertiary referral centres in New South Wales (NSW), Australia, which provided care for stroke patients in a geographically defined location with immediate CT access and on-site high dependency units (Australian National Stroke Unit Program Category A or B; n=20). ASUs in Category A have access to on-site neurosurgery whereas those in Category B do not.¹³ Patients were eligible if they spoke English, were aged 18 years or older, had a diagnosis of ischaemic stroke or intracerebral haemorrhage, and presented within 48 h of onset of symptoms to a participating ASU. Patients were excluded if they did not have a telephone or were admitted for palliative care.

Before randomisation, we recruited a pre-intervention patient cohort (July 30, 2005, to Oct 30, 2007) to provide a baseline sample before implementation of the intervention. Using identical procedures and instruments, we recruited a second post-intervention patient cohort (from Feb 4, 2009, to Aug 25, 2010) to provide a follow-up sample after intervention implementation. Informed written consent was obtained from the cluster guardian for ASU participation and from patients or their proxy for medical record access and participation in a telephone survey 90 days after hospital admission.

This trial was approved by the Human Research Ethics Committee of Australian Catholic University and the relevant ethics committees of all participating hospitals. The trial was governed by a steering committee including all investigators and an expert advisory committee consisting of independent researchers and stroke clinicians.

All outcome measures pertained to the individuals (patients) using methods previously validated for use by telephone (panel 1).¹⁴⁻¹⁶

Randomisation

ASUs were stratified by category (category A or B) and then by absolute numbers of pre-intervention cohort patients recruited (high or low recruiters). High recruiters had consented more than two patients per month; low recruiters two or fewer per month. De-identified stratification details were provided to an independent statistician who used random number generating software to randomise within strata with allocation concealed until provided to the Project Officer (SD) who assigned ASUs to their groups. Clinical research assistants masked to trial design enrolled patients. Patients were masked to ASU group allocation but clinicians delivering our intervention were not. Research assistants who undertook the computer-assisted telephone interviews and the medical record audits were masked to trial aims, design, and group allocation; the trial statistician was masked to group allocation.

Intervention

Our Fever, Sugar, Swallowing (FeSS) intervention targeted all ASU clinicians, focusing on barrier identification,²⁰ reinforcement of multidisciplinary teamwork,²¹ local adaptation,²² and use of site champions.²³ Using recommendations from Australia's national clinical guidelines for stroke,⁶ panels of experts developed clinical treatment protocols for management of fever, hyperglycaemia and swallowing for the first 72 h after ASU admission (panel 2). We aimed to trigger prompt nursing assessment and bedside treatment. Specifically, two team-building workshops were held to identify local barriers to multidisciplinary care²⁰ and enablers to implementation of the nurse-initiated treatment protocols. Two additional site-based interactive and didactic educational outreach meetings^{24,25} then were held for clinicians to discuss the protocols. Ongoing activities included site visits, telephone, and email support as reminders²⁶ (panel 2). ASUs in the control group received only an abridged version of existing guidelines.²⁷

The intervention ran from May 15, 2007 to August 25, 2010. Following implementation, we allowed a 3-month bedding down period to allow the FeSS protocols to become embedded into usual care before recruitment of the post-intervention cohort.

Data collection

An independent organisation was contracted to conduct computer assisted telephone interviews with patients

Panel 1: Primary and secondary outcomes

Primary outcomes: 90 days after hospital admission

- Death or dependency (dependency: modified Rankin Scale (mRS) ≥ 2)¹⁷
- Functional dependency [Barthel index (BI)]¹⁸
- Mean SF-36 mental component summary (MCS) score¹⁹
- Mean physical component summary (PCS) score¹⁹

We also undertook subgroup analyses by stroke severity.

Secondary outcomes: processes of care

- Mean temperature for the first 72 h after acute stroke unit (ASU) admission
- Mean finger-prick blood glucose for the first 72 h after ASU admission
- Proportion with swallowing screening undertaken within the first 24 h of ASU admission
- Discharge diagnosis of aspiration pneumonia (ICD 10)
- Length of hospital stay

90 days after hospital admission. The two interviewers underwent online training and competency assessment for modified Rankin Scale (mRS) administration.

Blinded retrospective medical record audits were undertaken using data documented prospectively. Four auditors obtained the following data: age, sex, stroke subtype (Oxfordshire Community Stroke Project classification),²⁸ time from onset of symptoms to ASU presentation; stroke severity (Los Angeles Motor Scale),²⁹ administration of thrombolysis, all temperature and blood glucose readings within the first 72 h of admission to an ASU, swallowing screening done within the first 24 h of ASU admission, and discharge diagnosis of aspiration pneumonia. Auditors attended a 2-day training programme. Two auditors abstracted data from 95% of medical records, enabling clarification of uncertainties. For quality assurance purposes, for the first 700 audits, 10% were re-audited with agreement occurring 95% of the time.

We calculated every patient's mean temperature and blood glucose for the first 72 h of their admission to the ASU and, using these, then determined a mean intervention and control ASU temperature and blood glucose. Three elements were required to meet the criteria for swallowing screening, namely, assessment of level of consciousness, cranial nerve assessment, and water-swallow test.

Statistical analysis

We used intention-to-treat analysis for all outcomes with SAS v9.2 software. The Barthel index is usually reported as a dichotomised variable but the cut points vary; we report both Barthel indexes of 60 or more and of 95 or more, the two most conventionally reported cut points to allow for comparison with published data.¹⁸ We summarised continuous and categorical data using conventional descriptive statistics. We adjusted all outcomes including the subgroup analyses for pre-intervention data and for clustering within ASUs using a logistic regression model fitted within a generalised estimating equation framework for dichotomous outcomes and a random intercept linear regression model for continuous outcomes. The linear and logistic models included the predictor variables of period (before and after), intervention and the interaction between period and intervention. The *p* value from the Wald test for the interaction term was used to see if the pre-post change in the intervention group was statistically different to the change in the control group. The CIs reported are those for the interaction term from the logistic or linear model but to obtain estimates of absolute difference, the models for dichotomous outcomes were refit with an identity link function. The *p* values for the interaction term from these models were almost identical to the logistic models. To control the type 1 error rate from the four primary outcome measures, our α level was set at 0.0125.

There were 19 clusters with a mean cluster size of 39 consenting patients in the pre-intervention cohort

Panel 2: Fever, sugar, swallowing (FeSS) intervention elements

Clinical treatment protocols for FeSS management by nurses for first 72 h of acute stroke unit (ASU) care: key elements

Fever

- Temperature monitored and charted every 4 h after admission to ASU for first 72 h.
- Temperature $\geq 37.5^{\circ}\text{C}$ treated with paracetamol (intravenous, per rectum, or oral), unless clinically contraindicated.

Sugar (hyperglycaemia)

- Formal glucose measured (venous blood not finger prick) on admission to hospital or admission to the ASU.
- Finger-prick blood glucose on admission to ASU.
- Finger-prick glucose every 1–6 h for first 72 h following ASU admission depending on previous blood glucose value.
- On admission, if blood glucose between 8 mmol/L and 11 mmol/L and patient is diabetic, or between 8 mmol/L and 16 mmol/L and patient is not diabetic, start saline infusion for 6 h.
- If, at any time in first 48 h after admission, blood glucose ≥ 11 mmol/L and patient is diabetic, or blood glucose ≥ 16 mmol/L and patient is not diabetic, start insulin infusion.

Swallowing

- Nurses underwent an education programme about dysphagia screening, which consisted of all nurses attending an in-service given by the speech pathologist using a DVD prepared specifically for this study.
- Nurses underwent a competency assessment before being able to screen patients, consisting of a pre-education and post-education written knowledge test, and a clinical competency test, completed on three patients and assessed by a speech pathologist.
- Patients were screened with the ASSIST tool by either a nurse who passed the competency test or a speech pathologist within 24 h of admission to ASU; the result of the screening was clearly documented in the patient's medical record by use of a sticker.
- Patients who failed the swallowing screening were referred to a speech pathologist for a swallowing assessment.

Site-based education and support

- Two multidisciplinary team-building workshops to identify local barriers and enablers to implement the FeSS nurse-initiated treatment protocols.
- Two site-based educational outreach meetings consisting of a standardised education programme about the FeSS treatment protocols delivered by the project officer (SD); Microsoft Powerpoint slides were left with the ASU nurse educator to be delivered to those who did not attend the meetings.
- Engagement of local stroke unit coordinators through support and feedback. The Project Officer (SD) visited each intervention ASU every 6 weeks, sent three monthly proactive emails to each site, and also instigated scheduled telephone follow-up every 3 months; all acted as reminders. She also responded to any site-based request for support if needed. Newsletters were sent out yearly.

(median 31; minimum 10; maximum 83). In the post-intervention cohort the mean cluster size was 59 consenting patients (median 58; minimum 13; maximum 145). We achieved our desired sample size consistent with our earlier statistical assumptions.⁹

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full

access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

19 (95%) ASUs agreed to participate (figure 1). The length of time ASUs had been established before trial commencement was similar between intervention and control groups. Data for the pre-intervention patient cohort have been published.¹⁰ Age, sex, 90-day death, 90-day death and dependency, 90-day functional dependency (BI), and health status (PCS score and MCS score) were similar for the intervention and control groups.

For the post-intervention cohort, of the 1292 eligible patients, 166 (13%) declined to participate (figure 2), resulting in 1126 (87%) consenting patients. Patients who agreed to participate were similar to those who did not consent in terms of age ($p=0.14$) and sex ($p=0.19$). There were no significant differences between consenting patients who provided full 90-day data and those who subsequently declined; 117 (10%) patients were lost to follow-up or withdrew (figure 2). There was no difference in the number of relatives who provided 90-day patient proxy outcome data between the intervention group (104 [19%]) and the control group (102 [24%]). Age, sex, pre-morbid level of dependency (mRS), stroke location, stroke severity, and time between onset of stroke symptoms and arrival at ASU were similar for patients in

the intervention and control groups although full-time employment seemed slightly lower in the control group (table 1). Only 77 (7%) received thrombolysis and most of these (60 [78%]) were in the control group.

After adjustment for baseline levels, patients from intervention ASUs were significantly less likely to be dead or dependent (mRS ≥ 2) at 90 days than patients from control ASUs ($p=0.002$; figure 3; table 2); the number needed to treat was approximately 6.4. 90-day mortality did not differ between patients from intervention (21 [4%] of 558) and control (24 [5%] of 451) ASUs ($p=0.36$) nor did the functional dependency (table 2). Patients from intervention ASUs were significantly more likely to have better SF-36 physical health scores indicating improved physical functioning; mental health scores did not differ between groups (table 2).

Our exploratory subgroup analyses by stroke severity showed that patients with a mild stroke (Los Angeles Motor Scale=0) from intervention ASUs were significantly less likely to be dead or dependent (mRS ≥ 2) at 90 days (56 [25%] of 226) than those from control ASUs (71 [39%] of 184; $p=0.02$) and reported better physical health than those from control ASUs (PCS score mean 48.3 vs 45.0; $p=0.008$). Similarly, patients with a more severe stroke (Los Angeles Motor Scale ≥ 1) from ASUs in the intervention group were significantly less likely to be dead or dependent (mRS ≥ 2) at 90 days (178 [54%] of 328) than those from control ASUs (181 [70%] of 260; $p=0.04$) and had better physical health (PCS score mean 43.6) than patients from control ASUs (40.8; $p=0.04$). Further, intervention ASU patients with more severe strokes were also less likely to have died at 90 days (17 [5%] of 328) than those from control ASUs (23 [9%] of 260; $p=0.001$).

With regard to processes of care, medical records were unavailable for 40 [4%] of the 1126 patients consented, resulting in collection of processes of care data for 1086 patients (table 3). Patients in intervention ASUs had a significantly lower mean temperature during the first 72 h of admission to the ASU compared with patients in the control ASUs (table 3). Post-hoc explanatory analyses showed a significant reduction in the number of patients from intervention ASUs who had at least one high ($\geq 37.5^\circ\text{C}$) temperature (table 3). Additionally, patients from intervention ASUs had significantly lower mean blood glucose during the first 72 h following ASU admission (table 3). Patients in intervention ASUs were significantly more likely to receive a swallowing screen within the first 24 h of ASU admission compared with patients in control ASUs (table 3). The prevalence of aspiration pneumonia did not differ between groups (13 [2%] of 603 in the intervention group vs 13 [3%] of 483 in the control group, $p=0.82$). The mean length of hospital stay did not differ between groups (table 3).

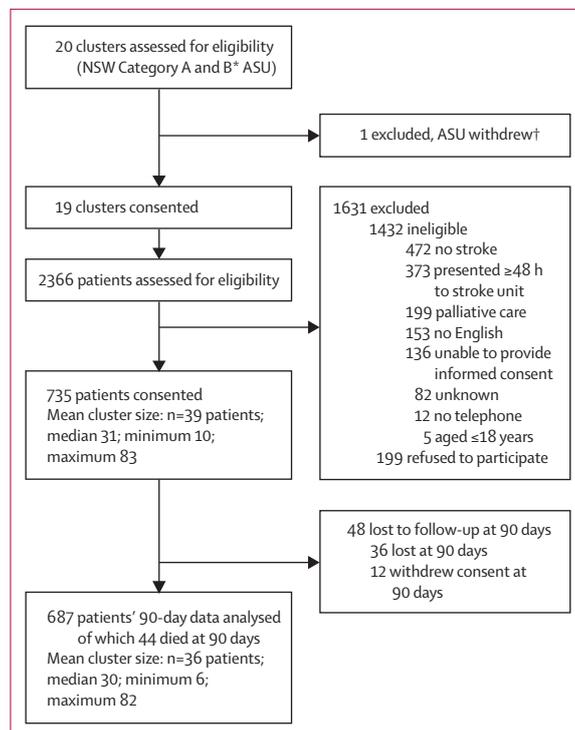


Figure 1: Pre-intervention trial profile

NSW=New South Wales. ASU=acute stroke unit. *Australian National Stroke Unit Program Category A or B correspond to stroke units with immediate CT access and on-site high dependency units; category B does not have on-site neurosurgery.¹³ †This cluster withdrew before recruitment of any patients.

Discussion

Our results show that patients of ASUs allocated to receive our multidisciplinary intervention to support proactive

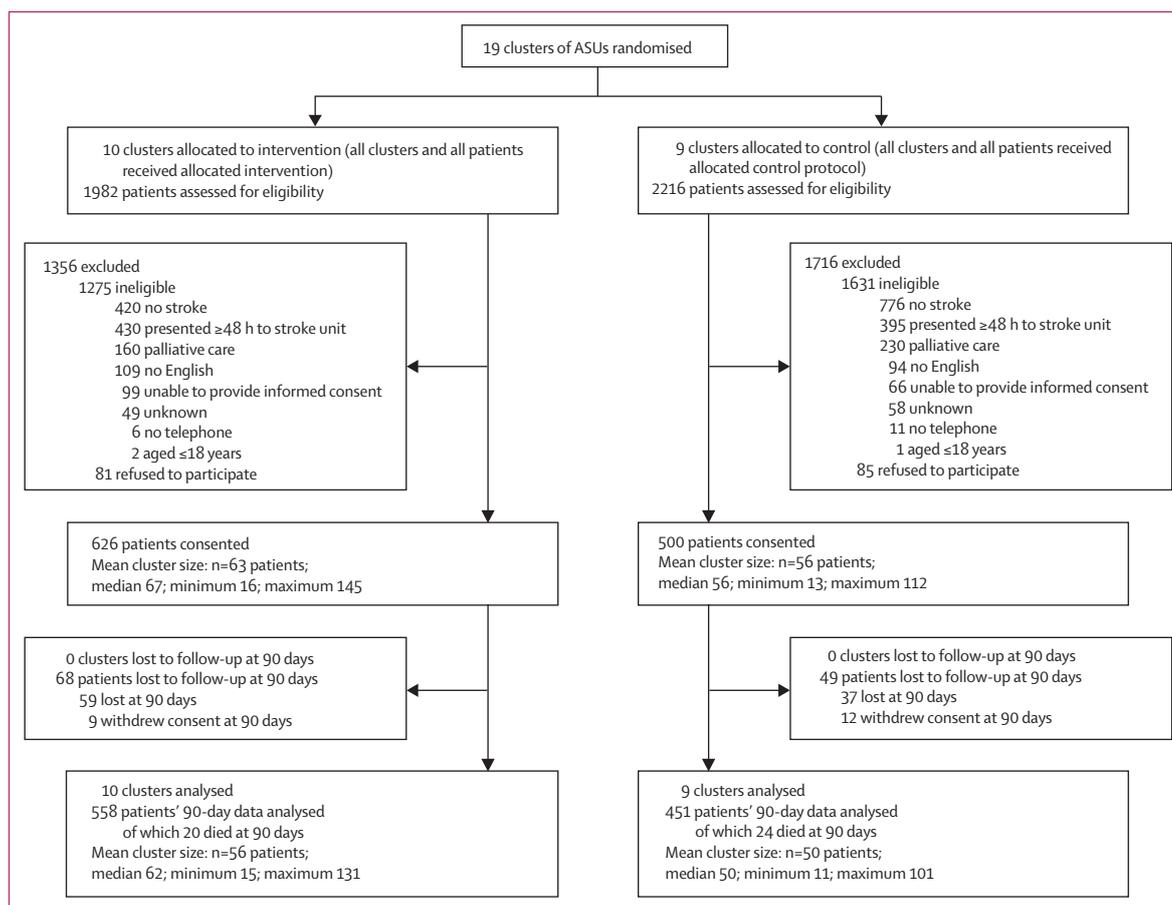


Figure 2: Post-intervention trial profile

evidence-based management of fever, hyperglycaemia, and swallowing were significantly more likely to be alive and independent at 90 days after admission. Specifically, we showed a 15.7% adjusted absolute difference in rates of 90-day death and dependency. The clinical significance of these results is more remarkable when compared against other established clinical and organisational interventions, namely administration of aspirin within 48 h,³⁰ stroke unit care,¹ and thrombolysis within 4.5 h.³¹ All deliver absolute benefit for independent survival of no more than 10%; all have higher numbers needed to treat (aspirin: 79;³⁰ stroke unit: 18;¹ thrombolysis: 8³² to 14³¹ depending on onset-to-treatment time) than our intervention to realise a benefit, with thrombolysis available only to a very specific ischaemic stroke population, unlike our intervention, which has relevance for all stroke patients. Hence, the 15.7% improvement and the number needed to treat of 6.4 reported with our FeSS intervention will be of immediate importance for clinicians, patients, and their carers.

Furthermore, our data show that patients from ASUs who received our intervention also had significantly improved processes of care. The mean temperature decreased significantly by 0.1 in intervention ASU patients

	Control (n=500)	Intervention (n=626)
Age group (years)		
<65	137/498 (28%)	195/625 (31%)
65–74	130/498 (26%)	150/625 (24%)
75–84	158/498 (32%)	181/625 (29%)
≥85	73/498 (15%)	99/625 (16%)
Sex		
Male	298/500 (60%)	376/626 (60%)
Female	202/500 (40%)	250/626 (40%)
Oxfordshire Stroke Classification Project (OCSP)		
Total anterior circulation infarct	27/296 (9%)	42/585 (7%)
Partial anterior circulation infarct	121/296 (41%)	298/585 (51%)
Lacunar infarct	82/296 (28%)	93/585 (16%)
Posterior circulation infarct	54/296 (18%)	113/585 (19%)
Intracerebral haemorrhage	12/296 (4%)	39/585 (7%)
Los Angeles Motor Scale		
0 (mild stroke)	203/493 (41%)	262/622 (42%)
≥1 (more severe stroke)	290/493 (59%)	360/622 (58%)
Aborigine or Torres Strait Islander		
Yes	6/425 (1%)	5/543 (1%)

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	Control (n=500)	Intervention (n=626)
(continued from previous page)		
Marital status		
Never married	20/425 (5%)	41/535 (8%)
Married	269/425 (63%)	323/535 (60%)
Widowed, divorced, or separated	136/425 (32%)	171/535 (32%)
Highest level of education		
No school certificate	145/424 (34%)	130/529 (25%)
School certificate	177/424 (42%)	187/529 (35%)
Higher school certificate	43/424 (10%)	93/529 (18%)
University, TAFE, or college	59/424 (14%)	119/529 (22%)
Employment status*		
Retired	297/425 (70%)	357/535 (67%)
Employed full-time	28/425 (6.6%)	74/535 (14%)
Permanently unable to work or ill	60/425 (14%)	43/535 (8.0%)
Employed part-time or casual	18/425 (4.2%)	46/535 (8.6%)
Unemployed, home duties, volunteer work, or student	22/425 (5.2%)	15/535 (2.8%)
Premorbid mRS*		
No symptoms at all	376/425 (88%)	477/537 (89%)
No significant disability despite symptoms	18/425 (4.2%)	18/537 (3.4%)
Slight disability	18/425 (4.2%)	22/537 (4.1%)
Moderate disability	11/425 (2.6%)	18/537 (3.4%)
Moderately severe disability	2/425 (0.5%)	2/537 (0.4%)
Time from onset of symptoms to ASU (min)		
Mean (SD)	826 (701)	953 (648)
Data are n (%) unless otherwise stated. ASU=acute stroke unit. mRS=modified Rankin scale. TAFE=technical and further education. *Percentages might not total to 100% because of rounding.		
Table 1: Demographic and clinical characteristics of the post-intervention cohort		

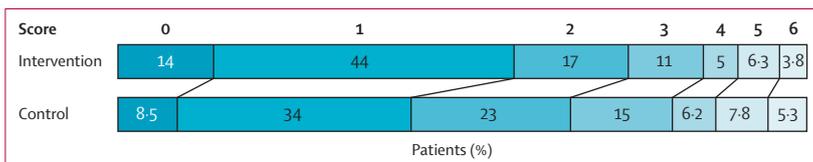


Figure 3: Distribution of 90-day modified Rankin scale*
*Percentages may not total to 100% due to rounding.

and, although this small difference occurred within the afebrile temperature range, our analyses incorporated all patients, including those who never had a fever, making this change all the more potentially important. That there were fewer patients with fever in the intervention group also is of interest, possibly because of improved observation and early intervention. The mean blood glucose also significantly decreased in patients receiving care in intervention ASUs, showing the positive effect of our intervention on glucose management.

Although the proportion of swallowing screenings attended was significantly higher in patients from intervention ASUs when compared with patients from control group ASUs, the absolute performance appears low. We used very conservative screening criteria, however, and intentionally did not capture screening occurring outside the ASU, nor swallowing assessments that could also have had a screening component occurring within 24 h of admission. Although not shown to be significant, the promise of reduced length of stay also could represent substantial savings for hospitals.

Despite being implemented with multidisciplinary support from physicians, speech pathologists, and nurses, our clinical protocols were delivered by bedside nurses. Protocol-led care enabled nurses to be proactive in their management of fever, hyperglycaemia, and swallowing. Role delineation within multidisciplinary teams has clear benefit for patients, ensuring that critical physiological variables are monitored and managed. We are confident that future interventions to change behaviour could still further raise the quality of care received by stroke patients in Australian hospitals. Replicability of our intervention would enable wider implementation in other ASUs with clinical leadership and change management provided by stroke networks and non-government organisations such as stroke charities.

On a methodological note, we achieved excellent engagement (19 of the 20 NSW ASUs), also recruiting large cohorts of patients with a modest proportion of loss-to-follow-up (10%). Of note, our death and dependency results remained significant ($p=0.004$) when a sensitivity analysis was undertaken where we assumed all patients lost to follow-up were dead or disabled ($mRS \geq 2$). Our extension of the data endpoints to

	Group		p value*	Difference in absolute change (95% CI)
	Control (n=451)	Intervention (n=558)		
Death and dependency ($mRS \geq 2$) (ICC 0.018)	259/449 (58%)	236/558 (42%)	0.002	15.7% (5.8 to 25.4)
Barthel index ≥ 95 (ICC 0.015)	254/423 (60%)	367/532 (69%)	0.07	9.5% (-0.5 to 19.5)
Barthel index ≥ 60 (ICC 0.009)	380/423 (90%)	487/532 (92%)	0.44	2.5% (-3.6 to 8.6)
SF-36 Physical health (PCS score) (ICC 0.026)	42.5 (10.5)	45.6 (10.2)	0.002	3.4 (1.2 to 5.5)
SF-36 Mental health (MCS score) (ICC 0.011)	49.4 (10.6)	49.5 (10.9)	0.69	0.5 (-1.9 to 2.8)
Data are number (%) or mean (SD). ICC=intracluster correlation. mRS=modified Rankin scale. PCS=physical component summary. MCS=mental component summary. *p values are for the interaction term between intervention group and time period (pre-intervention or post-intervention) and adjusted for clustering within acute stroke unit.				
Table 2: Primary outcomes 90 days after hospital admission				

	Group		p value*	Difference in absolute change (95% CI)
	Control (n=483)	Intervention (n=603)		
Fever				
Mean temperature during first 72 h in ASU (°C, ICC 0.084)	36.6 (0.30)	36.5 (0.27)	0.001	0.09 (0.04 to 0.15)
At least one temperature $\geq 37.5^{\circ}\text{C}$ in first 72 h (ICC 0.009)	131 (27%)	105 (17%)	<0.0001	16.4% (8.3 to 24.6)
Glucose				
Mean glucose during first 72 h in ASU (mmol/L; ICC 0.056)	7.0 (2.0)	6.8 (1.8)	0.02	0.54 (0.08 to 1.01)
Swallowing screening				
Swallowing screening within 24 h of admission to ASU (ICC 0.156)†	24/350 (7%)	242/522 (46%)	<0.0001	29.2% (22.0% to 36.4%)
Length of hospital stay (days)	13.7 (12.7)	11.3 (10.3)	0.144	1.5 (-0.5 to 3.5)

Data are number (%) or mean (SD). ASU=acute stroke unit. ICC=intracluster correlation. *p values are for the interaction term between intervention group and time period pre-intervention or post-intervention and are adjusted for clustering within ASUs. †Excludes those screened in emergency department.

Table 3: Secondary outcomes, processes of care measures for fever, glucose, and swallowing screening

encompass both 90-day patient outcomes and processes of care is exceptional in stroke research and we encourage similar scope in future studies.

Similar to many acute stroke studies,³³ our study was limited in that patients with severe strokes were under-represented. This under-representation was probably due to our deliberate exclusion of patients with severe stroke who were for palliation only. Exclusion of these patients also might account for the non-significant differences between groups in functional dependency and mortality. However, our subgroup analyses showed significant improvements for death and dependency outcomes for both mild and severe strokes in our intervention group (14% in the mild stroke cohort and 16% in the more severe stroke cohort) showing a clear benefit for both mild and more severe strokes.

Other opportunities to improve patient outcomes have emerged. Prompt recognition of stroke in emergency departments and better triage are crucial for those eligible for thrombolysis, and if new treatments such as the FeSS intervention or early rehabilitation³⁴ are to be started, then timely admission to an ASU is imperative.³⁵ As our intervention focused on care of patients admitted to ASUs, our findings are not necessarily generalisable to stroke patients cared for in general medical wards. They also are only generalisable to patients admitted to ASUs within 48 h of symptom onset and who receive the protocol-led care for the first 72 h after admission to an ASU. Because access to a stroke unit for all stroke patients is not always achievable and delays often occur, we recommend future trials to examine the effect of similar multidisciplinary interventions in general wards and emergency departments.

Our trial provides compelling evidence that better management of fever, hyperglycaemia, and swallowing in acute stroke patients during the initial 72 h of admission to an ASU can result in decreased rates of death, dependency, and improved processes of care. Further, our trial is one of the few to clearly show the effect of good

Panel 3: Research in context

Systematic review

In the first days of an acute stroke, temperature above 37.5°C occurs in 20–50% of patients; up to 68% of patients become hyperglycaemic; and 37–78% experience dysphagia, resulting in increased morbidity and mortality and enlarged infarct size. We searched Medline and CINAHL databases for reports in English (no other restrictions) using the search term "stroke" (all inclusive) combined with: "fever"; "pyrexia"; "hyperthermia"; "hyperglycaemia"; and "glucose" and found no systematic reviews of treatments to effectively manage either physiological variable. Similarly, we also combined the term "stroke" with "dysphagia", "swallow/ deglutition", and "swallowing disorders/deglutition disorders". Evidence from a systematic review³⁶ showed that stroke patients with dysphagia are at risk of pneumonia and that this risk is higher in patients who aspirate. Use of a formal dysphagia screen can decrease the risk of pneumonia. Additionally, no studies have examined the combined effect of systematic management of fever, hyperglycaemia, or swallowing. International guidelines recommend monitoring and prompt treatment of these three variables. No effective treatment exists, however, with which to change bedside care and ensure multidisciplinary teams comply with evidence-based clinical practice guidelines. Systematic reviews of strategies with this goal in mind persistently argue that more implementation research is needed to identify effective strategies and to ensure resources are not wasted on activities of questionable value. In response, our research tested a multidisciplinary intervention designed to raise standards of care in acute stroke units with a cluster randomised controlled trial. Barrier identification,²⁰ educational meetings,^{24,25} use of local opinion leaders,³³ and reminders²⁶ have shown promise in earlier studies in diverse clinical settings and we incorporated these elements in our intervention and assessed long-term patient outcomes of 90-day death and dependency. We also examined processes of care.

Interpretation

The QASC trial provides high-quality evidence that a guideline implementation strategy to support multidisciplinary teamwork and good nursing care focused on evidence-based management of three key physiological variables in ASUs delivers significantly better post-discharge outcomes for stroke patients. Clinical leaders of stroke services can adopt this strategy with confidence that their outcomes will improve.

nursing care on death and dependency. Additionally, it is one of the first implementation trials in acute stroke to harness the stroke unit network in Australia (panel 3). To our knowledge, it is also one of the largest multidisciplinary

rigorously evaluated interventions in acute stroke. The importance of our intervention lies in its ability to augment the benefits of stroke unit care. Further research as to its potential to benefit stroke patients unable to access immediate stroke unit care and also its value for populations other than stroke is warranted.

Contributors

SM, as chief investigator conceived, designed, obtained funding, supervised the study and wrote the first draft of the report. CL, JW, JMG, RG, CDE, NWC, ME, DC, and CQ helped conceive, design, and obtain funding for the study. SD coordinated the study and supervised data collection. PD assisted with data collection. SM, CDE, PM, JMG, CL, SD, and PD assisted with data analyses. SM, CDE, and PM had complete access to the data. SM, JW, JMG, CDE, PM, NWC, and CL assisted with data interpretation. All authors contributed to subsequent versions of the report and had responsibility for the decision to submit for publication.

Conflicts of interest

We declare that we have no conflicts of interest.

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