

Leaving a legacy of stroke in Europe: A community of dedicated professionals is changing the face of stroke in Europe

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A B S T R A C T

Time is of the essence in the treatment of acute stroke; however, there are wide variations, across and within countries, in the ability to hospitalize, scan, diagnose, and treat acute stroke patients rapidly within the accepted time window of 4.5 hours. Door-to-needle (DTN) time is an important performance indicator that illustrates the speed and operational efficiency of stroke units. Significant progress is being made; DTNs often exceeded an hour only a few years ago, but can now be achieved in under seven minutes in leading stroke units. This symposium examined the strategies and contributory factors that result in reduced DTN times, and how these strategies can be more widely implemented. The Quality in Acute Stroke Care (QASC) programme in Australia has shown the incorporation of standardized nurse-led treatment protocols for the management of fever, hyperglycaemia, and dysphagia (FeSS protocols) significantly improve outcomes for stroke patients. European evaluation of these protocols, in collaboration with ESO and the ANGELS initiative, and potentially leading to their adoption in European acute stroke treatment practice is discussed.

Key words: acute stroke, door-to-needle, FeSS protocols, QASC

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INTRODUCTION

This symposium had two main components. The first was a focus on how stroke neurologists and their hospital teams can improve the implementation of evidence-based practices in the treatment of acute stroke. In particular, success factors that have led to significant reduction in delays, such as door-to-needle time (DTN), in leading stroke centres, were identified. This provides an adoption model and a basis for simulation training in centres trying to reduce their own in-hospital delays. The second component examined how nurse-led protocols to manage fever, hyperglycaemia, and dysphagia have significantly improved outcomes for stroke patients in the Quality in Acute Stroke Care (QASC) programme in Australia, and provided an update on how the QASC programme will be evaluated throughout Europe.

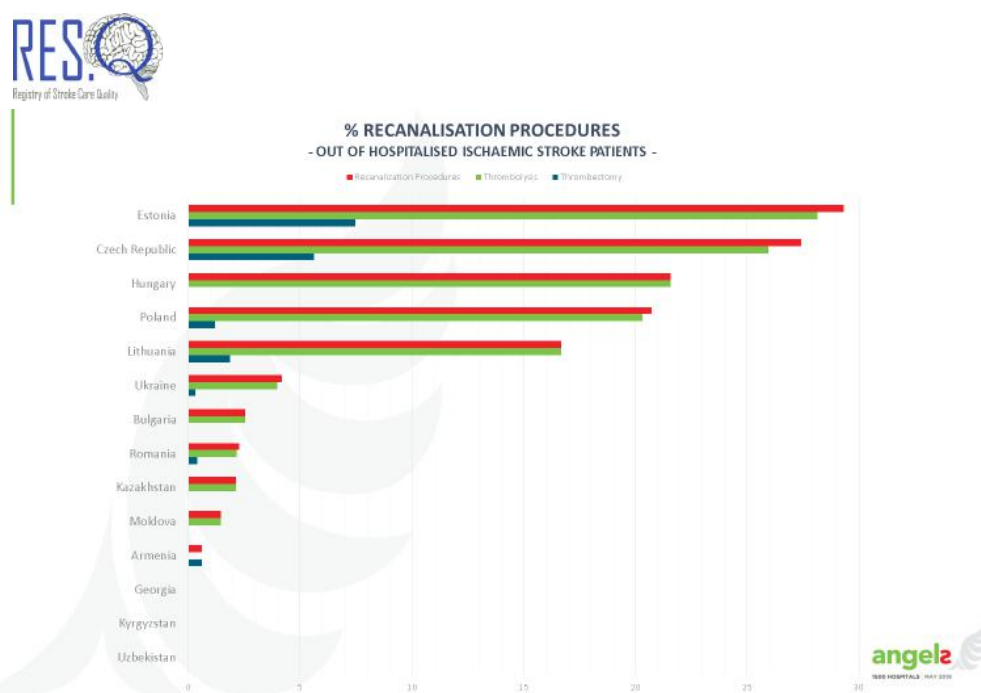
THE ANGELS INITIATIVE – MORE STROKE CENTRES, MORE PATIENT DATA, AND GREATER IMPLEMENTATION OF EVIDENCE-BASED TREATMENTS.

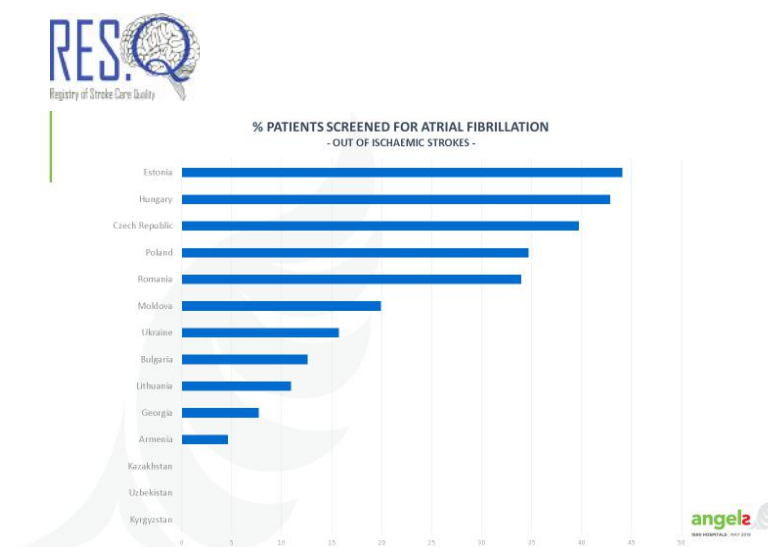
Established by Boehringer Ingelheim in 2015, in collaboration with international stroke experts, the **A**cute **N**etworks **S**triving for **E**xcellence in **S**troke (ANGELS) is now operational in more than 30 countries, and is officially endorsed by two leading global stroke organizations: WSO and ESO, and many National stroke societies. The principal objective of ANGELS is to improve the treatment of acute ischaemic stroke by providing stroke teams with the tools, resources, and support they need to set up and to optimize stroke networks. Twenty or 30 years ago, treatments for acute stroke were very limited; however, since then, there have been a raft of advances, with more patients treated in purpose-built stroke units and the emergence of effective life-saving treatments, especially IV thrombolysis and mechanical thrombectomy. Additionally, hemicraniectomy and neurointerventions in cerebral aneurysms and arteriovenous malformation (AVM) have advanced considerably. Acute stroke treatment has therefore moved from an era of no or limited treatments, to the use of some of the most effective treatments and interventions available in medicine. However, implementation of evidence-based treatments for acute stroke is not consistent within and across European countries. In many hospitals and countries patient assessments are not consistent and effective treatments (such as IVTP and mechanical thrombectomy) cannot be accessed.

Newly emergent data from RES-Q illustrate the disparity in the percentage of recanalization procedures conducted in ischaemic stroke patients in Eastern European countries.

Similarly, the percentage of acute stroke patients currently screened for atrial fibrillation (AF) in Eastern Europe shows considerable variation: <5% in Armenia, but approaching 45% in Estonia.

Currently, less than a third of stroke patients are treated in dedicated stroke centres, and the ANGELS initiative vision is for all stroke patients to receive the same level of treatment wherever they live in Europe. The ESO Quality Improvement Programme, through the ANGELS initiative, is engaging with hospitals and encouraging them to apply for partnership, with the aim of building a minimum of 1,500 specialist stroke centres and stroke-ready hospitals. All participating centres will contribute to patient data registries, and will receive feedback that will allow them to compare the performance of their centre with other participating centres. Improving centres will now receive ANGELS awards and stroke unit certification based on the standard of care provided to their stroke patients. Two approved national registries will collate patient data. The established SITS (Safe Implementation of Treatment in Stroke) database; this is a leading platform for high quality stroke data, currently for over 170,000 patients in over 1,600 stroke centres, and the more recently established RES.Q (Registry of Stroke Care Quality). RES.Q has been developed specifically as a quality of care improvement tool, and captures metrics including: whether hospitalization occurred in a stroke unit, availability of CT scanning, screening for AF, warfarin usage etc. Accordingly, RES.Q will record the impact of more consistent adherence to evidence-based treatments and interventions.





Use of registry data provides information on the extent and quality of stroke care at individual centres and at national level. For example, in Czech Republic, registry data show leading stroke centres are now conducting recanalization procedures in 50% of ischaemic stroke patients, and screening for AF takes place in over 90% of patients in the leading centres. Registry data also provide the basis of the ESO ANGELS awards to participating centres. The criteria for centres applying for these awards are shown below.

ESO certification is intended to provide a strong motivational impetus within European stroke units and hospitals with expert acknowledgement of improvements in stroke care achieved. The ESO Stroke Unit and Stroke Centre Certification platform for European institutions was launched during the 2016 ESO Congress in Barcelona and is currently accepting applications for certification. This certification process will provide an objective assessment of clinical excellence, and aims to improve the quality of stroke patient care by reducing variation in

	Gold Award	Platinum award	Diamond Award
	Registration criteria met	Registration criteria met	Registration criteria met
% of patients treated with DTN time <60 mins	50%	75%	75%
% of patients treated with DTN time <45 mins	-	-	50%
% Recanalization rate out of total stroke incidence in hospital	5%	15%	25%
% of all suspected stroke patients that received CT or CAT scan	80%	85%	90%
% of ischaemic stroke patients with antiplatelet therapy at discharge	80%	85%	90%
% of AF-related stroke patients discharged with anticoagulants	80%	85%	90%
% of all stroke patients undergoing dysphagia screen	80%	85%	90%
Patients treated in a dedicated stroke unit or ICU during their stay	-	-	Yes

clinical processes. Certification is anticipated to provide an important benchmark for assessment of the quality of stroke management.

The ANGELS initiative is on track to reach the target of 1,500 stroke-ready hospitals by 2019.

With an increasing number of European hospitals and stroke centres operating under the ANGELS umbrella,

and with more centres demonstrating greater certified compliance with ESO stroke management guidelines, a more consistent approach to the delivery of higher quality care in acute stroke is anticipated. This, in turn, should lead to improved outcomes for stroke patients, and to a reduction in the mortality and morbidity burden imposed by ischaemic stroke in many European countries.

OUR GOAL: 1,500 STROKE-READY HOSPITALS BY 2019 WHERE ARE WE NOW?



REDUCING IN-HOSPITAL DELAYS: THE IMPORTANCE OF EXEMPLAR CASE STUDIES AND SIMULATION TRAINING

Finland is currently taking a lead position in reducing hospital door-to-needle times (DNT), with Turku University Hospital, for example, reducing median DNT from 31.5 minutes in 2013, to 10.5 minutes in 2016. Even shorter DNTs of 4-6 minutes have been achieved using a streamlined emergency admission procedure starting with the stroke neurologist receiving a code stroke prenotification alerting call from emergency medical service (EMS). During patient transfer to hospital, availability of electronic records allows the patient's comorbidity status, medications, and most recent laboratory parameters to be reviewed, and the CT scanning team and laboratory nurse are alerted. With patient arrival, the neurologist makes further rapid assessments of any upper and lower limb impairments, gaze diversion, facial paresis, dysarthric speech or aphasia, to determine if the NIHSS score is high enough to warrant thrombolysis. Point of care (POC) testing to determine INR and rapid transfer to the CT scanner follows. Preparation and conducting the CT scan represents the longest delay

to DNT; typically, this takes 2-3 minutes. Examination of the scan by the neurologist to rule out bleeding or other contraindications to IVT then takes place, and the decision to give thrombolysis taken. The patient is informed of the potential risks and benefits of treatment as the rt-PA is prepared, and the initial bolus followed by infusion is administered. At this point a full NIHSS assessment is carried out and the patient transferred to the Angiography suite in the case of a large vessel occlusion.

POINTERS FOR REDUCING DNT: THE 10-STEP FINLAND EXPERIENCE

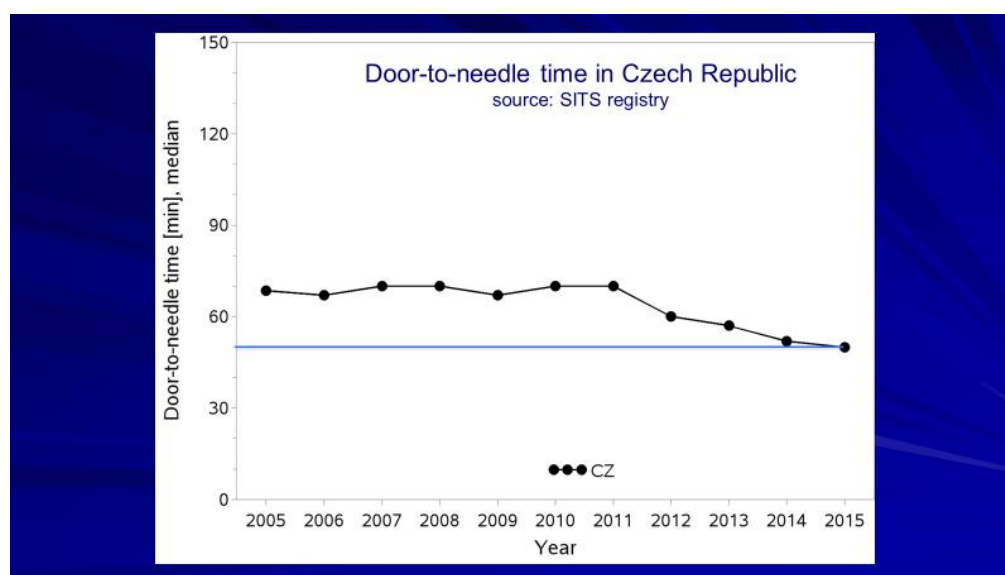
1.	Availability of a protocol for IV thrombolysis and intra-arterial treatments (IAT)
2.	Hands-on training for the neurologists on call
3.	Education and cross-train ER nurses and CT scanning personnel
4.	Single call stroke code prenotification system
5.	Ever-ready CT scanner on stand-by. Use only for acute patients.
6.	Brief neurological examination
7.	Prioritize POC INR – don't wait for other laboratory results
8.	rt-PA bolus after plain CT
9.	With large vessel occlusion evident in CT Angiograph – after rt-PA bolus transfer the patient directly to the Angio suite
10.	Follow-up of results.

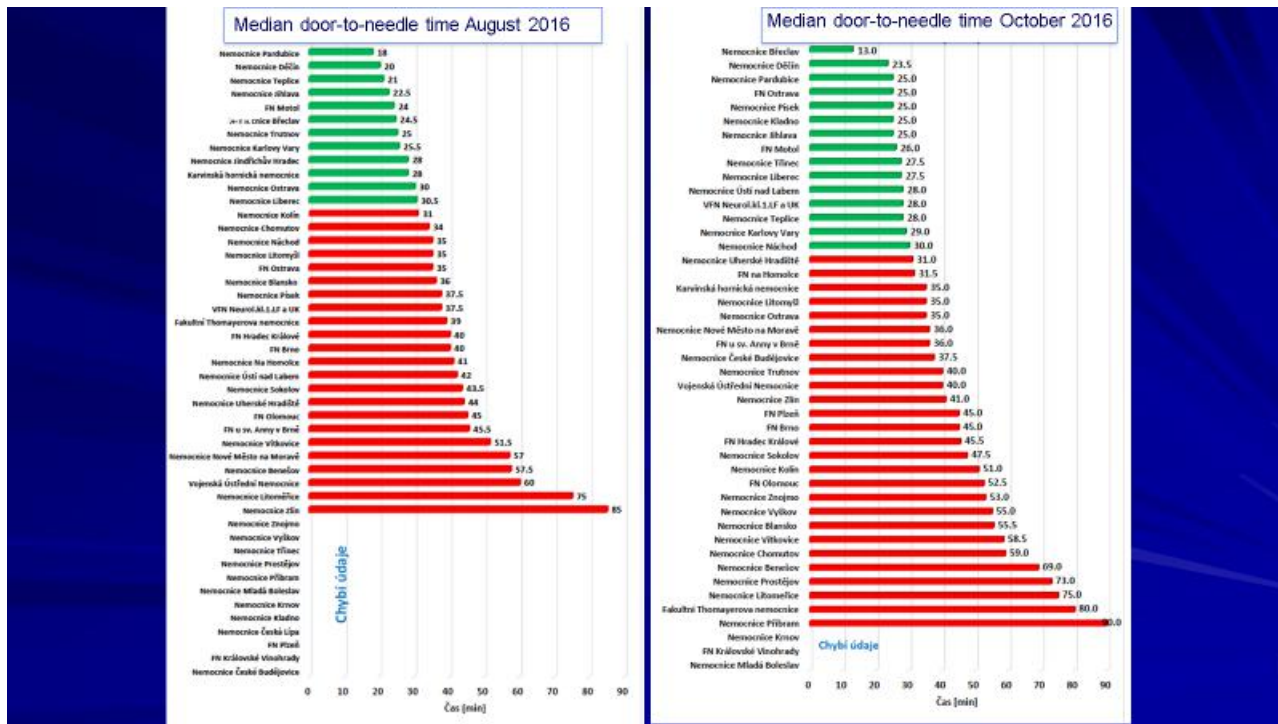
The modus operandi and clinical logistics of patient delivery, assessment, diagnosis, and treatment of acute stroke, as practised in Finland, is largely applicable in other countries where acute stroke patient care is often delivered outside of comprehensive stroke centres. Video evidence from Slovakia provided by Dr. Miroslav Brozman shows that by adopting as many elements of the Finnish model as is possible, delays are minimized, and DNT can be achieved in under seven minutes. One area where time can be gained is making the best use of the time when the patient is en route to the hospital. Good communication is crucial to ensure all members of the hospital's acute stroke team are alerted, and have prepared the CT scanner in readiness. In this case study, the rapid exclusion of intracranial haemorrhage was rate determining; it confirmed the patient was eligible for IVT, allowing the IV bolus of rtPA to be administered six minutes and 50 seconds after the patient had arrived at the hospital.

TRAINING TO AVOID DELAYS IN DOOR-TO-NEEDLE TIME – THE CZECH AND SLOVAK EXPERIENCE

The efficacy of treatment for acute stroke is affected by the duration between stroke onset and treatment administration. In particular, reduction in DTN is associated with better treatment outcomes. SITS registry data show that the median DTN value in Czech Republic, during the period 2005-2011, remained relatively constant, and in excess of 60 minutes.

In August 2016, the Czech Stroke Society began monthly reporting of DTN times at all Czech stroke centres, and, in parallel, began a programme of simulation training with the aim of reducing DTN time. This involved video recording of the training sequences that were then streamed to an expert training panel for analysis and feedback to course participants. By October 2016, the number of centres achieving a DTN of ≤ 30 minutes had increased, reflecting an increased motivation to improve DTN performance.





To date, around 100 healthcare professionals (neurologists, radiologists, emergency physicians and nurses) have received DNT simulation training in the Czech and Slovak Republics. Questionnaire feedback, using a 0-100% scale, showed course attendees considered the training to be 85% relevant to performing thrombolysis correctly, 90% of physicians scored the training at 90% relevant for reducing DNT (nurses 72%), and impact on improvement in team communication was scored at 77%.

Furthermore, these same comparisons, based on SITS 2017 data, show further continued improvements were achieved in Czech Republic compared with other countries in 2017.

Czech SITS registry data for 2016 based on over 3,000 patients who received rt-PA showed that median stroke onset to treating hospital/door time was 85 minutes. However, all timing comparisons in Czech Republic (Country), versus all SITS centres, for door to imaging time, door to treatment needle time, and stroke onset to treatment were lower in Czech Republic than in all SITS centres.

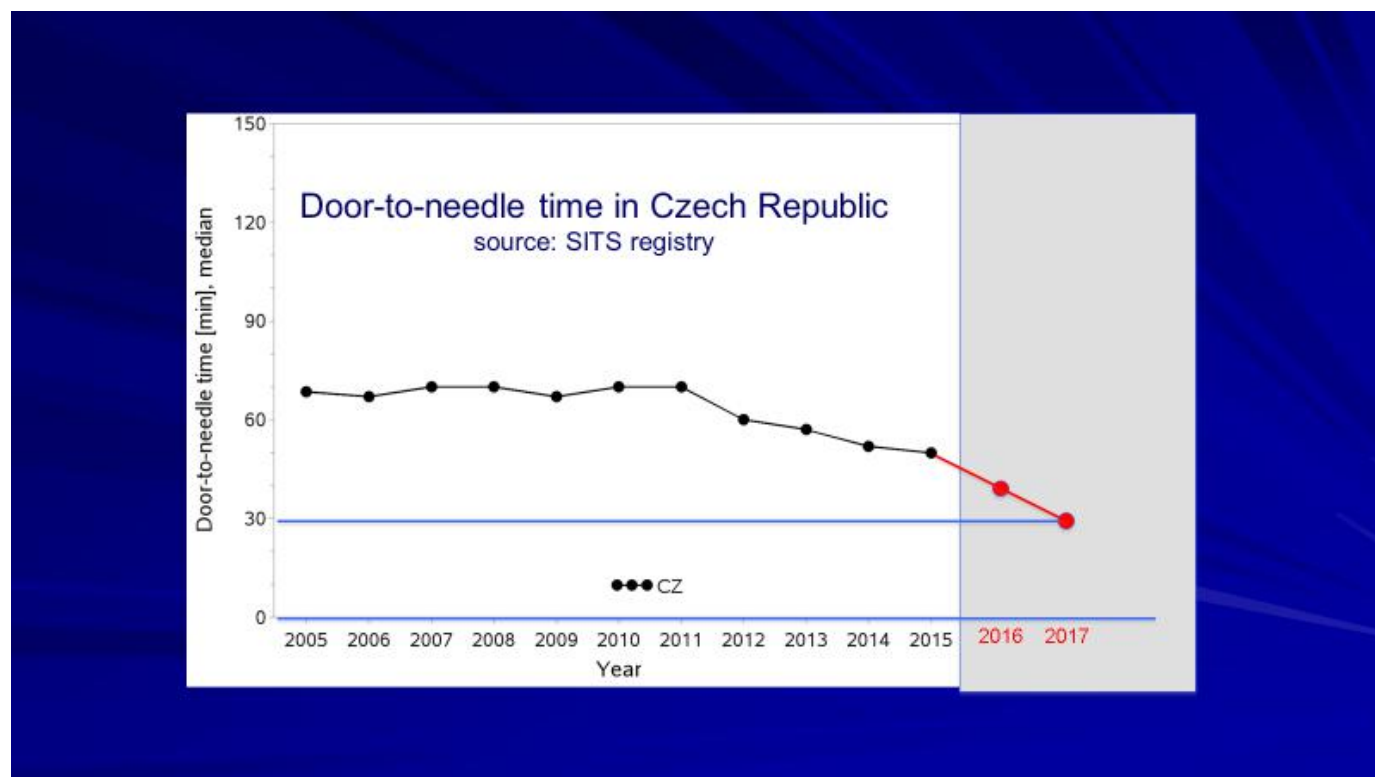
Time delay (minutes)		Centre	Country	All centres
Stroke onset to treating hospital/door time	Median		85.0	81.0
Door to imaging study time	Median		17.0	25.0
Door to treatment/needle time	Median		40.0	62.0
Stroke onset to treatment/needle time	Median		130.0	156.0

TREATMENT LOGISTICS CZECH REPUBLIC VERSUS OTHER COUNTRIES: SITS REGISTRY IN 2017

Time delay (minutes)		Centre	Country	All centres
Stroke onset to treating hospital/door time	Median		85.0	82.0
Door to imaging study time	Median		11.0	24.0
Door to treatment/needle time	Median		30.0	57.0
Stroke onset to treatment/needle time	Median		120.0	155.0

The introduction of a multi-tool programme with acute stroke simulation training including on-course video feedback, and reporting of response performance data, allowing between-centre comparisons, is having a very tangible effect in reducing DTN, and other delays, in the Czech Republic. Notably, the median DTN time has been reduced by over 50% in the 6-year period from 2011 to 2017.

Simulation training was well accepted by course participants, and considered highly relevant for improving the logistics of immediate in-hospital management of patients with acute stroke. There is now a pressing requirement to investigate the full potential of simulation training to reduce delays, and to document this clearly. The Czech Republic is now in pursuit of a “20-20” goal for the year 2020. This is to achieve a 20% rate for thrombolysis, and to reduce the median DTN time to 20 minutes.



THE QUALITY IN ACUTE STROKE PROJECT (QASC) COMESTO EUROPE

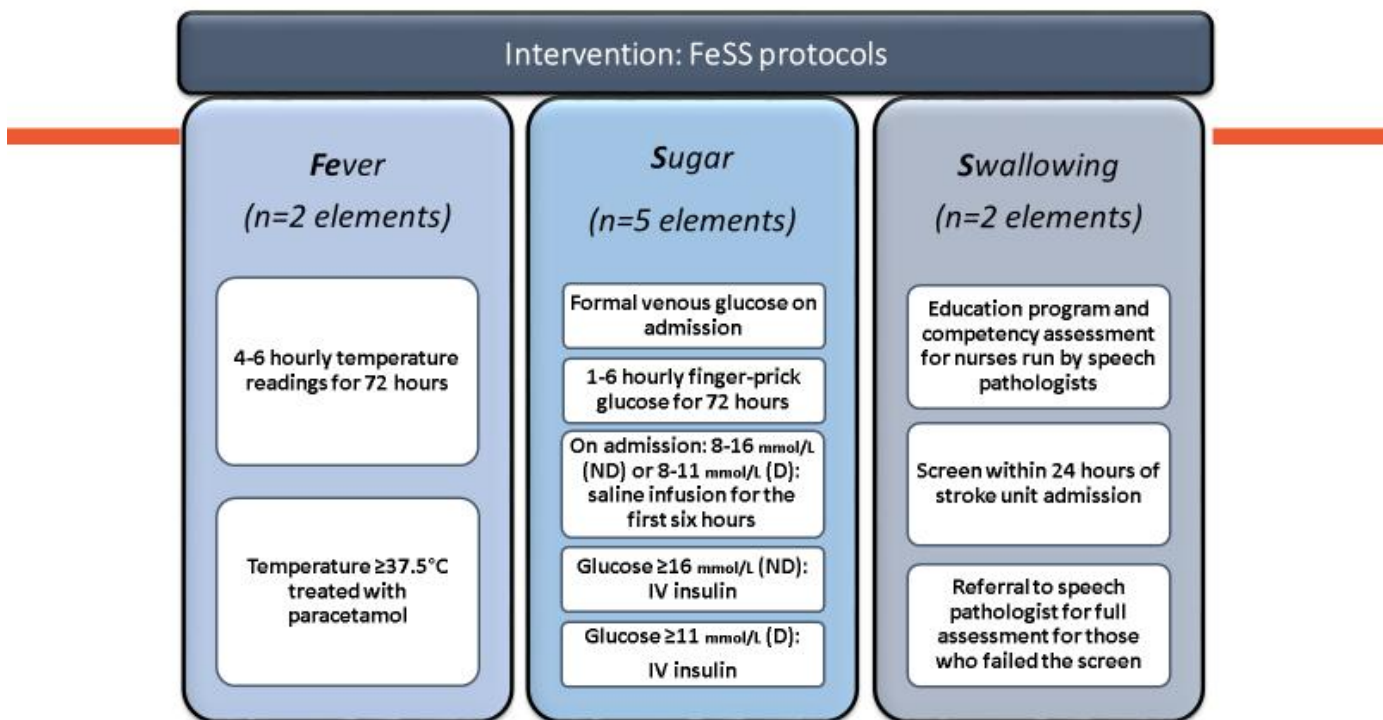
A focus on fever, hyperglycaemia and dysphagia

Incorporating three simple protocols in nursing care to manage fever, hyperglycaemia, and swallowing can lead to profound improvements in outcomes in stroke patients. Up to a third of patients have a temperature >37.5° C following stroke onset. This is associated with a marked increase in morbidity and mortality, and is an indicator of poor prognosis. Meta-analysis of pooled data from six cohort studies in ischaemic stroke confirmed that fever, within the first 24 hours of hospitalization, is associated with a doubling of the odds of short-term mortality (Prasad 2010).

Hyperglycaemia occurs in up to 45% of patients in the first 48 hours following stroke onset. Blood glucose > 8 mmol/L predicts increased mortality and poorer functional outcome, and significantly, hyperglycaemic non-diabetic patients hospitalised for stroke are three times more likely to die than those who are not hyperglycaemic (Capes et al., 2001).

The importance of dysphagia screening in acute stroke patients has been highlighted by a recent analysis of Ontario Stroke Registry data (Joundi et al., 2107). This analysis revealed that approximately one in five of ischaemic stroke patients were not screened for dysphagia, and failure to screen was associated with poor outcomes, notably: in-hospital pneumonia, severe disability (Modified Rankin Score 4-5), discharge to long-term care, and increased 1-year mortality. It was also evident that these poorer outcomes occurred in patients who had suffered a mild stroke.

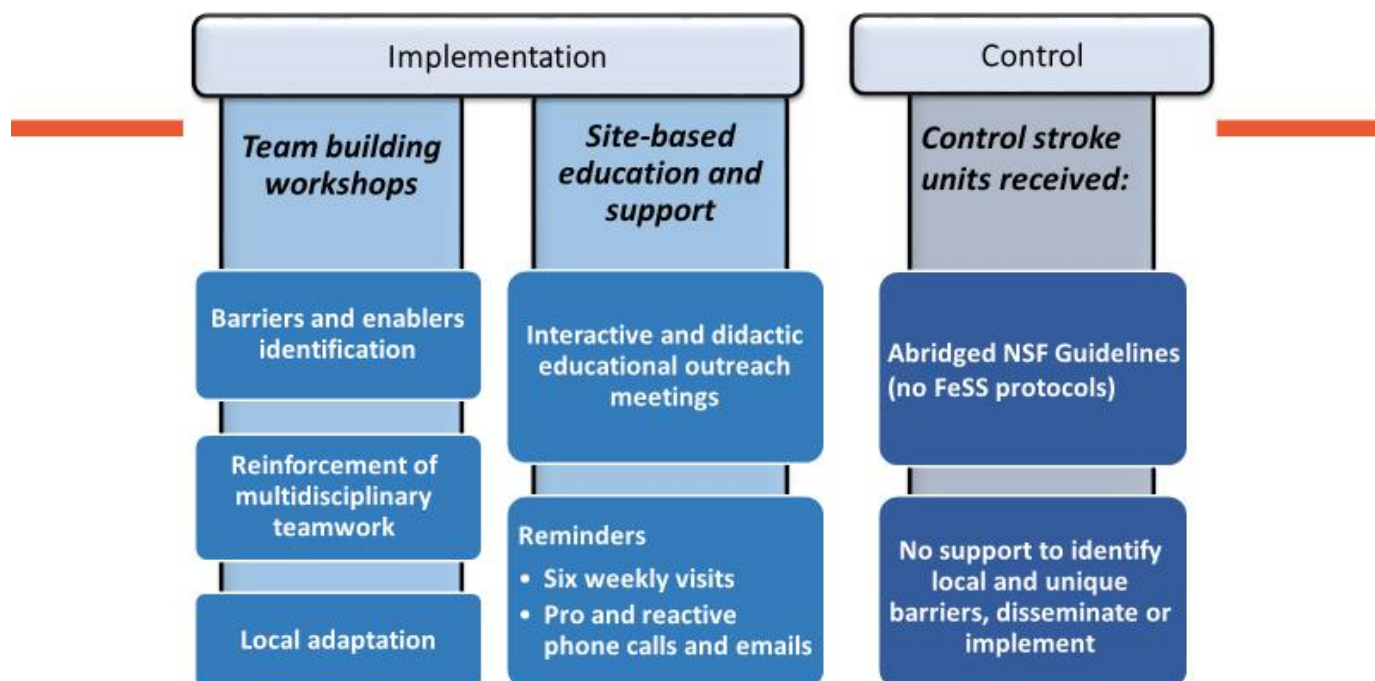
The goal of improving fever, hypoglycaemia and dysphagia in acute stroke patients is to reduce the ischaemic penumbra and to prevent core stroke damage extending into the penumbra. To this end, the randomised, controlled, Quality in Acute Stroke Care (QASC) trial was conducted in Australia. This study developed and tested a way to implement three protocols aimed at improving fever, hyperglycaemia, and dysphagia management in acute stroke (Middleton et al., 2011). The key nurse-led interventions of the **F**ever, **S**ugar, **S**wallowing (FESS) protocols are illustrated below.



Middleton S, McElduff P, Ward J, Grimshaw JM, et al. *Lancet* 2011;378(9804):1699-1706.

All FeSS interventions were conducted during the first 72 hours following the patient's admission to the participating stroke hospital. To support the implementation of the FeSS protocols, a programme of team building and site-based education and support was established (shown

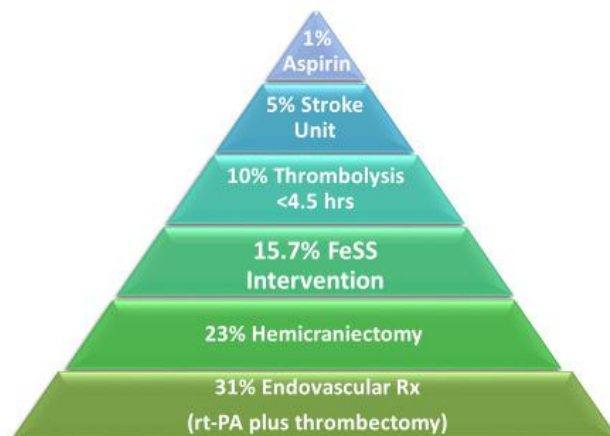
below). Control stroke centres, with no FeSS participation, did not receive this support. Only local National Stroke Foundation Guidelines were provided.



The 19 stroke units in New South Wales that implemented the FeSS protocols demonstrated a 15.7% reduction in death and mRS-measured disability, at 90 days, compared with control centres ($p=0.002$). Implementation of the FeSS protocols also led to significant decreases in mean temperature ($p=0.001$), blood glucose ($p=0.02$) and improved swallow screening ($p\leq 0.001$). Additionally, hospital stay was reduced by a non-significant but

clinically important two days ($p=0.14$). These relatively simple interventions when implemented carefully and consistently during the initial 72-hour of hospitalization are responsible for substantial improvements in outcomes for stroke patients. Hence, the relative contribution and clinical significance of FeSS protocols, in comparison with other acute stroke treatments and interventions, is illustrated in the following diagram.

Clinical Significance

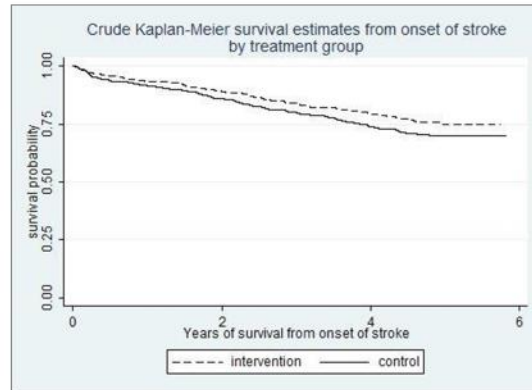


Dhamija RK, et al. *Aust Fam Physician* 2005;36(11):892-895.

Long-term follow-up, in over 1,000 QASC patients, over four years, has shown that patients in the FeSS intervention arm in QASC were >20% less likely to die compared with patients in the control arm (p=0.045; adjusted HR = 0.77,

CI:0.59-0.99). Kaplan-Meier survival estimate curves for patients in both the FeSS intervention and control groups, showing early separation, are illustrated below.

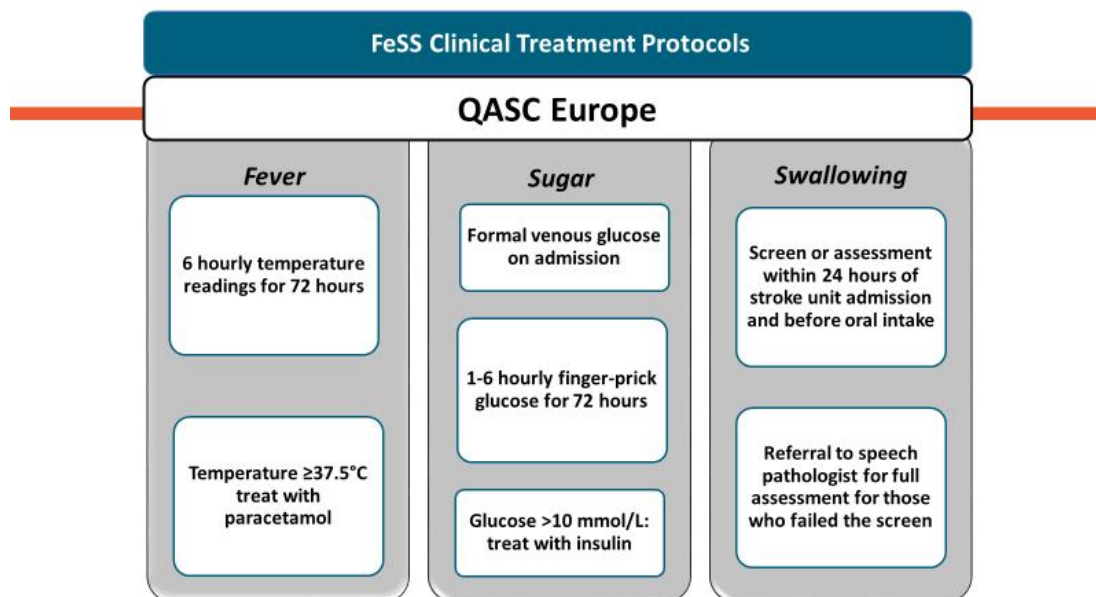
Results



Middleton S, Coughlan K, Mnatzaganian G, et al. *Stroke* 2017;48(5):1331-1336.

These data demonstrate implementation of nurse-initiated multidisciplinary FeSS protocols for the management of fever, hyperglycaemia, and swallowing dysfunction, reduced 90-day death and dependency, and have the potential to reduce long-term mortality after discharge from stroke units. Subsequently, FeSS protocols have been implemented in all 36 stroke units in New South Wales. This process involved the conduct of pre- and post-intervention medical record audits. As a result, significantly increased proportions of patients have received care according to FeSS protocols. Inclusion of FeSS protocols in future stroke management guidelines, especially for hospitals that are unable to provide the most advanced stroke services, is recommended.

Expansion of the QASC programme into Europe is now underway, in collaboration with the Boehringer-Ingelheim ANGELs initiative and the European Stroke Organisation. Key objectives are to implement the FeSS clinical protocols across stroke services in Europe, to evaluate the success of uptake of these protocols, and to characterize any comprehensive lessons from translating evidence-based results, on a large scale, across multiple countries. Some simplification of the hyperglycaemia algorithm has been undertaken for FeSS protocol use in Europe. This is shown below.



QASC Europe will not be a clinical trial, but the stepped-wedge design and staged approach of the project represents the best way to implement evidence. All hospitals already participating in the ANGELS initiative are eligible for recruitment. Eligible sites will therefore:

- Implement the FeSS clinical protocols as part of routine stroke care;
- Nominate clinical stroke site champions, trained to act as local change agents;
- Routinely record temperature, glucose and swallow screening practices;
- Conduct medical record audits at pre-defined time points;
- Have access to a computer and the internet.

Recruitment of QASC Europe is now underway and project developments will be fully documented at the earliest opportunity.

CONCLUSIONS

Avoidance of delays in the hospitalization and treatment of acute stroke patients continues to be a major challenge; however, significant progress is being made in the reduction of door-to-needle times, and other delays that impede rapid and most appropriate treatment. Video recording of well executed acute stroke admission, CT scanning, and treatment sequences are providing useful models for simulation training, and for improving communication within stroke teams and emergency services. The expansion of European stroke patient registries, and increased reporting of outcomes at the level of individual stroke centres, provides benchmarking opportunities, and is increasing motivation for improvement. Emerging initiatives, notably, ANGELS and Quality in Acute Stroke Care (QASC) Europe project, are helping to improve the implementation of evidence-based care for stroke patients. Relatively simple interventions, as illustrated by the FeSS protocols, when applied consistently and at the right time, have demonstrated a remarkable effect in significantly improving outcomes for stroke patients. Evaluation and implementation of FeSS protocols across Europe is anticipated to make a major contribution to improving the quality of stroke care, and ultimately the quality of life for recovering stroke patients.

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