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TACTICS - Trial of Advanced CT Imaging and Combined Education Support for Drip and Ship: evaluating the effectiveness of an 'implementation intervention' in providing better patient access to reperfusion therapies: protocol for a non-randomised controlled stepped wedge cluster trial in acute stroke

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ABSTRACT

Introduction Stroke reperfusion therapies, comprising intravenous thrombolysis (IVT) and/or endovascular thrombectomy (EVT), are best practice treatments for eligible acute ischemic stroke patients. In Australia, EVT is provided at few, mainly metropolitan, comprehensive stroke centres (CSC). There are significant challenges for Australia's rural and remote populations in accessing EVT, but improved access can be facilitated by a 'drip and ship' approach. TACTICS (Trial of Advanced CT Imaging and Combined Education Support for Drip and Ship) aims to test whether a multicomponent, multidisciplinary implementation intervention can increase the proportion of stroke patients receiving EVT.

Methods and analysis This is a non-randomised controlled, stepped wedge trial involving six clusters across three Australian states. Each cluster comprises one CSC hub and a minimum of three primary stroke centre (PSC) spokes. Hospitals will work in a hub and spoke model of care with access to a multislice CT scanner and CT perfusion image processing software (MIStar, Apollo Medical Imaging). The intervention, underpinned by behavioural theory and technical assistance, will be allocated sequentially, and clusters will move from the preintervention (control) period to the postintervention period.

Strengths and limitations of this study

- This trial is one of the few rigorously designed, large-scale implementation intervention trials in acute stroke care targeting predominantly smaller hospitals without an established research culture, using a localised context-fit implementation approach.
- The study design involves establishment of site readiness and local context during baseline to facilitate tailoring of the implementation intervention, which will be jointly delivered by members of the research team and the cluster coordinator to the cluster environment, while maintaining the underlying function of the intervention, thereby enhancing the relevance of the implementation without compromising fidelity.
- The implementation intervention, informed by the theoretical domains framework, will use emerging virtual reality technology to teach multidisciplinary, collaborative, non-technical acute stroke workflow optimisation skills to staff working in acute stroke care, while removing known barriers to professional development opportunities for staff in regional and rural Australia by utilisation of a stand-alone training approach that can be completed anytime anywhere.

Strengths and limitations of this study

- The trial will embed multimodal imaging technology and knowledge management strategies within existing infrastructure, protocols and pathways using a 'hub and spoke' model of care to support complex decision making in smaller centres with a junior and rotating clinical workforce.
- As the implementation of endovascular thrombectomy hub and spoke models of care is at an early stage in Australia, random allocation of the study intervention will not be feasible within the timeframe of the study, therefore introducing potential selection bias.

Primary outcome Proportion of all stroke patients receiving EVT, accounting for clustering.

Secondary outcomes Proportion of patients receiving IVT at PSCs, proportion of treated patients (IVT and/or EVT) with good (modified Rankin Scale (mRS) score 0–2) or poor (mRS score 5–6) functional outcomes and European Quality of Life Scale scores 3 months postintervention, proportion of EVT-treated patients with symptomatic haemorrhage, and proportion of reperfusion therapy-treated patients with good versus poor outcome who presented with large vessel occlusion at spokes.

Ethics and dissemination Ethical approval has been obtained from the Hunter New England Human Research Ethics Committee (18/09/19/4.13, HREC/18/HNE/241, 2019/ETH01238). Trial results will be disseminated widely through published manuscripts, conference presentations and at national and international platforms regardless of whether the trial was positive or neutral.

Trial registration number ACTRN12619000750189; UTNU1111-1230-4161.

BACKGROUND

Context of acute stroke care in Australia

In Australia, there were an estimated 38 000 stroke events in 2017,[1] and in 2018, 8400 people died due to stroke, accounting for 5.3% of all deaths.[1] In 2015, national stroke variables[2] and indicators for acute stroke care[3] were introduced to track performance and context variables over time. The Australian health system provides universal coverage and most acute stroke care is provided at publicly funded primary and comprehensive stroke centres. People living in socioeconomically disadvantaged areas (over-represented rurally) report a higher prevalence of cardiovascular diseases (6.4% vs 4.8%) compared with those in the least disadvantaged areas.[1] Regional and rural stroke centres often serve a large geographical area, sometimes across jurisdictional boundaries, are frequently staffed by a younger and more transient workforce, have less access to senior expertise, and have less routine use of guidelines, protocols and care plans for stroke, compared with centres in major cities. To facilitate systems improvements and knowledge retention within such centres, some hospitals use nursing-led models of care,[4] which can shorten acute stroke treatment times;[5] however, these are challenging to implement in complex medical environments without sufficient high-level support.[6] A nurse practitioner can provide advanced clinical care and thus has the potential to alleviate medical workload; however, this role is underutilised.[7]

Use of stroke reperfusion for acute stroke in Australia

Intravenous stroke thrombolysis (IVT) is one of few evidence-based treatments for ischemic stroke,[8–10] but uptake has been slow,[11] relating to the complexity of assessment for treatment and the urgency of administering IVT within 4.5 hours of stroke onset, which requires coordinated interprofessional and interdepartmental collaboration, access to senior neurology staff for decision assistance, confidence and acceptance of treatment risk.[12] Recent trials[13 14] have shown that treatment can be extended to 9 hours according to clinical and brain perfusion imaging criteria; however, without accurate identification of stroke characteristics, some patients receive little or no benefit from IVT.[15]

The use of endovascular thrombectomy (EVT) for acute stroke patients with a large vessel occlusion (LVO) within 24 hours of stroke onset has been a guideline-approved treatment in Australia since 2018,[16] supported by results of multiple recent trials.[17–23] EVT is recommended to patients with LVO based on specific clinical and imaging criteria indicating the presence of salvageable brain tissue, with IVT administered while concurrently assessing suitability for EVT.[16] Provision of EVT requires a wide range of specialised staffing, services and infrastructure, including highly skilled nursing and interventional neuroradiology professionals, high procedural volumes, and access to an advanced brain imaging and angiography suite. These constraints mean that, in Australia, EVT is predominantly provided in larger metropolitan centres, with only 10 hospitals providing a 24/7/365 EVT service that fulfil the national criteria of a comprehensive stroke centre (CSC),[24] which includes establishing partnerships with local hospitals. In 2019, there were 91 hospitals with the ability to offer thrombolytic therapy 24/7; however, most of these centres reside in major cities.[25] In such a geographically dispersed country, this results in a significant degree of inequity in access for patients living in regional or rural areas.

Utilisation of advanced imaging to guide treatment decision

Many regional and rural stroke services rely only on non-contrast CT (NCCT) scans to determine treatment eligibility; however, NCCT does not accurately identify which patients are suitable for EVT.[26] By undertaking advanced imaging with multimodal CT or MRI, physicians are able to positively identify stroke,[27] LVO and the likelihood of salvageable tissue.[28] A large body of work has demonstrated that by using perfusion imaging it is possible to estimate the volume and location of irreversibly damaged tissue (ischemic core) and potentially salvageable ischemic tissue (penumbra) with computed tomography perfusion (CTP).[29] This information can be used to identify reperfusion treatment responders (small core, large penumbra) as well as those where reperfusion therapy may be futile (large core).

The advantages of multimodal CT over MRI are its speed of acquisition, wide availability and limited patient exclusions: a multimodal stroke imaging protocol can be

performed in 5 min for a comprehensive evaluation of the extracranial and intracranial circulation, the amount of infarcted brain tissue and the size of the penumbra,[30] compared with MRI which is relatively inaccessible and therefore not used as first-line acute stroke imaging in Australia, with the exception of paediatric stroke. The diagnostic utility of CTP cannot be overemphasised, especially when patients may be assessed by less experienced or expert clinicians. Utilisation of such technology in regional and rural Australia is possible but requires changes to processes of care and increased access to imaging interpretation through telestroke or hub and spoke arrangements.[12]

Optimising the acute stroke workflow to improve access to EVT for regional and rural Australians

In Australia, approximately two-thirds of thrombectomy patients are referred from other metropolitan or rural hospitals.[31] In rural areas, delays to the initiation of thrombectomy are generally between 4 and 6 hours.[32] Even in urban areas, interhospital transfers are often slow, with a median transfer time of 2 hours.[33] Furthermore, patients who initially present to an EVT-capable centre generally experience a waiting time of at least 60 min between hospital arrival and when thrombectomy can be performed.[34] However, studies conducted at larger metropolitan centres[35 36] indicate that it is possible to reduce treatment times for acute stroke reperfusion, but few studies report on successful time-saving strategies in regional and rural hospitals.[37] A recent retrospective review highlighted that higher-volume endovascular stroke centres had faster treatment times, better reperfusion rates and improved clinical outcomes,[38] and shorter EVT treatment times have been associated with increased chances of good patient outcomes.[38–40] A quality improvement programme in the state of Victoria has shown that it is possible to obtain a median door in door out (DIDO) time of <60 min[41] for EVT transfers from a metropolitan primary stroke centre (PSC) using a hub and spoke model of care, and a study in rural New South Wales points towards transport modality (air vs road) and associated procedures as important predictors of faster DIDO times.[32] While DIDO target times have been developed for myocardial infarction, there is currently no consensus-based DIDO target time for acute stroke.

To improve access to best evidence stroke reperfusion care in regional and rural Australia, there are three main components that warrant attention: optimisation of the stroke reperfusion workflow, teaching non-technical workflow skills from a multidisciplinary and collaborative perspective, and utilisation of available expertise via innovative technology and models of care. TACTICS (Trial of Advanced CT Imaging and Combined Education Support for Drip and Ship) will use these strategies as part of a broader practice improvement implementation intervention.

METHODS AND DESIGN

Aims

The study aims to test whether a multicomponent, multidisciplinary implementation intervention can increase the proportion of stroke patients receiving EVT.

The following are the study objectives:

- To evaluate the effectiveness of an implementation intervention combining multimodal CT imaging, streamlined workflows, triage, transport and reperfusion pathways and protocol training in providing patients better access to stroke reperfusion therapies.
- To assess the potential clinical impact of the implementation intervention.

Trial status

The baseline phase in cluster 1 commenced on 13 May 2019, with the implementation intervention commencing on 12 August 2019. The trial is currently being rolled out in cluster 4. The anticipated completion date of the trial (eg, last case entered into the trial data set) is 31 December 2023. The trial was submitted prospectively to the Australian New Zealand Clinical Trials Registry (ANZCTR) on 10 April 2019 and was registered on 20 May 2019. Analysis of trial results has not commenced.

Trial design

This is a non-randomised, stepped wedge, cluster trial of an enhanced model of care combining the establishment of multimodal CT brain imaging capability and streamlined workflows in PSCs (spokes) supported by a metropolitan or regional CSC (hub). Sites are allocated to their 'step' on a convenience basis (ie, not randomised). Each cluster will progress through three phases: the first phase will be the preintervention baseline (control) phase, the second phase will be the 3-month active intervention phase immediately following introduction of the intervention package, and the third phase will be a postintervention period of 3–6 months, with an additional 3 months for collection of outcome data (see figure 1). Each cluster (a hub and spoke network) will sequentially receive the multicomponent, multidisciplinary collaborative implementation intervention of support tools and resources: within-cluster contrasts between preintervention and postintervention periods will be made. Automated imaging analysis software is an essential element of this implementation effectiveness trial and will be available at all sites prior to baseline. The implementation intervention will be delivered in accordance with local variations in context, set-up and need.[42 43]

Patient and public involvement

A patient with lived experience of stroke is a core member of the TACTICS research team and has been involved with the conceptual design and roll-out of study elements.

Sample, participants and setting

The trial sample will involve six clusters, each cluster comprising one hub and a minimum of three spokes, with a total of 38 hospitals across the Australian states of

Cluster 1 Baseline	**Cluster 1** Intervention	**Cluster 1** Post-intervention					
	Cluster 2 Baseline	**Cluster 2** Intervention	**Cluster 2** Post-intervention				
		Cluster 3 Baseline	**Cluster 3** Intervention	**Cluster 3** Post-intervention			
			Cluster 4 Baseline	**Cluster 4** Intervention	**Cluster 4** Post-intervention		
				Cluster 5 Baseline	**Cluster 5** Intervention	**Cluster 5** Post-intervention	
					Cluster 6 Baseline	**Cluster 6** Intervention	**Cluster 6** Post-intervention

Figure 1 Stepped wedge model. Each study phase (baseline, intervention and postintervention) is 3 months.

New South Wales, Queensland and South Australia (see figure 2). Most spoke hospitals will be regional PSCs with a multislice CT scanner capable of CTP and a stroke care unit or equivalent staffing, for example, stroke physician and stroke nurse coordinator. Spoke hospitals will refer appropriate acute stroke cases to an EVT-designated CSC and work in a 'hub and spoke' model of care (ie, using a drip and ship programme). A list of participating sites can be obtained on reasonable request by contacting the corresponding author.

Intervention allocation and blinding

Clusters will be allocated to the study intervention sequentially on a convenience basis. Clusters will be enrolled in close liaison with the research team, hospital executives, governance officers, hospital staff and relevant stakeholders.

Hospital staff will not be blinded to the intervention allocation as they are participating in the study intervention, but will be asked not to distribute the learnings from the implementation intervention to other hospitals outside of their cluster.

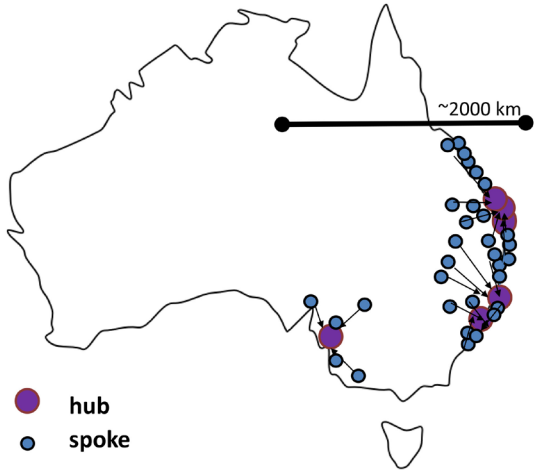

Figure 2 Map of participating hub and spoke hospitals.

Trial recruitment

Eligible hospitals were identified from the Stroke Foundation and stroke clinical network data. Each hub will be contacted by acute stroke leaders in the research team to discuss and provide support for the study at their hospital and within their catchment, to verify eligibility and to confirm what PSCs in the hub catchment are eligible to participate in the study. Clinical leaders will then contact spokes in each catchment to discuss the study, confirm eligibility, provide in principle support and invite them to participate. Consent for the study will be sought from the hospital executive and the site principal investigator via a Clinical Trial Research Agreement (CTRA) between the research team and the participating hospital. The CTRA will specify the purpose of the study, the requirements and the responsibilities of each party, and acknowledge the ongoing strategic relationship between the parties for the purpose of conducting the trial.

Data collection

Collection of case data

Throughout the course of the trial, each participating hospital will be asked to enter consecutive and prospective case data into a centralised data set, hosted on the International Stroke Perfusion Imaging Registry cloud-based platform. Case data will be entered by a trained health professional (site data manager) at each hospital and will include cases 18 years and above who are treated with stroke reperfusion (IVT and/or EVT). The trial will provide support to each hospital for the manual data entry into the TACTICS electronic case report form (eCRF). Data elements will include age, sex, premorbid modified Rankin Scale (mRS), stroke subtype using the Oxfordshire Community Stroke Project classification,[44] stroke risk factors, stroke severity using the 15-item National Institutes of Health Stroke Scale (NIHSS) score[45] at baseline and up to 72 hours post-treatment, process times such as door to needle, DIDO, door to groin puncture times and interhospital transport times, whether patients

arrived by ambulance, multimodal imaging profile, stroke reperfusion treatment, interhospital transfer of care, post-treatment measures such as Thrombolysis in Cerebral Infarction score, haemorrhage transformation, discharge data, and death.

Consent and assent

Opt-out patient consent

The trial will use an opt-out consent process for collection of demographics, clinical and 90-day outcome data on patients receiving reperfusion therapy (numerator data). Patients will be provided with an opt-out form and a reply-paid envelope (addressed to the hospital) by hospital staff prior to discharge (see online supplemental file 1). Patients who have not received the opt-out form prior to discharge will be mailed the form postdischarge. Opt-out rates will be recorded by the site data manager at each hospital, monitored by the trial data manager, and are anticipated to be around 2%–6% based on opt-out rates reported by the Australian Stroke Clinical Registry.[46] Although case data will not be collected for patients opting out, the number of opt-outs per hospital will be noted for the purpose of cross-checking data completeness.

Waiver of patient consent

A waiver of consent approach has been established to allow inclusion of de-identified case data in instances where patients passed away prior to receiving the opt-out documentation.

Training of data managers at participating hospitals

The trial data manager will liaise with site data managers at participating hospitals about data variables and processes for data entry. This will include completion of data for episodes presenting to both hub and spoke sites, opt-out consent and waiver of consent requirements, and technical support as needed. Regular data monitoring will be set up to ensure timely and accurate data collection in the eCRF, with specific emphasis on capturing the patient journey for patients who have presented to a spoke hospital and then transferred to the hub for potential EVT. The trial data manager will do regular monitoring to determine case completion and prompt timely collection of outcome data at 90 days post-stroke.

Process for collecting outcome data 90 days post stroke

Collection of mRS functional status at 90 days post stroke is part of the recommended best practice care, but it is not routinely collected by smaller hospitals and those without an established research culture. Therefore, the trial will support sites to collect outcome measures by facilitating access to mRS training and providing a per-patient payment for this activity.

Outcome data will be collected by trained staff via a telephone call to treated patients (IVT and/or EVT) using the 7-point (0–6) mRS and the EuroQoL 5-Dimension 5-Level (EQ-5D-5L). Hospital staff will enter de-identified follow-up data directly into the TACTICS eCRF. Both the mRS and the EQ-5D-5L measure include a set of checklist questions to enable consistency of data collection.

Data safety monitoring

This is an implementation trial and thus does not require a data safety monitoring committee. There were, however, extensive consultations at the design stage to determine relevant data elements and mechanisms.

Interim analysis, stopping rules, adverse events and auditing of trial conduct

There will not be an interim analysis of study outcomes as this is an implementation trial. Any adverse or unintended effects resulting from the trial intervention or implementation will be dealt with according to hospital-specific guidelines for reporting of incidents and adverse events. Given the quality improvement focus of the trial and no direct contact with patients as part of the intervention, no adverse events are anticipated. The conduct of the trial will be in accordance with Good Clinical Practice requirements.

Participant retention

If a hospital decides to stop participating in the trial due to unforeseen circumstances, no replacement hospital will be recruited unless this adversely impacts on the eligibility of the cluster to participate in the study. If key staff stop participating in the trial, then new staff will be recruited as outlined in the CTRA.

Measures and outcomes

Primary outcome: proportion of patients treated with EVT (comparing baseline with the 3–6 months postintervention phase)

The proportion of all stroke patients receiving EVT, adjusted for clustering, will be assessed using de-identified case data entered into the TACTICS eCRF by staff at each participating hospital. Denominator data will be the International Classification of Diseases-10th Revision (ICD-10) Australian Modification (AM) coding of all stroke separations using cluster denominator data. The primary outcome will be measured at the end of the 3–6 months postintervention period.

The trial *numerator* will be all patients treated with EVT at the designated CSC (hub), including spoke to hub and direct to hub presentations. The numerator is entered by participating sites and thus not independent or blinded.

The trial *denominator* will be all strokes (ICD-10-AM I61s, I62.9, I63s and I64). Denominator data will be obtained in collaboration with regional or jurisdictional health authorities of the total case load (all strokes) per hospital per unit timeframe from ICD-10 coding of all admitted stroke separations. The denominator of all strokes was chosen to provide a consistent measure across hospitals and jurisdictions. It is based on medical coding collected via regional or jurisdictional registries and thus independently coded and blinded.

Box 1 Secondary outcomes

- Proportion receiving IVT at spoke hospitals, using denominator data for all spokes/cluster. This outcome will be assessed using de-identified case data entered into the TACTICS eCRF by hospital staff at each participating spoke hospital (numerator). Denominator data will be ICD-10 coding of all stroke separations for all spokes in a cluster.
- Proportion with good functional outcome (mRS 0–2) or poor functional outcome (mRS 5–6) of all patients treated with IVT at spoke hospitals.
- Proportion of reperfusion therapy-treated patients with good functional outcome (mRS 0–2) or poor functional outcome (mRS 5–6) who presented with LVO at spoke sites.
- Proportion with good functional outcome (mRS 0–2) or poor functional outcome (mRS 5–6) of those treated with EVT per cluster, measured at hub, including direct to hub patients and spoke to hub patients.
- Proportion of stroke patients treated with EVT who had an EQ-5D-5L utility score indicating good health at 3 months post-treatment, measured at hub, including direct to hub patients and spoke to hub patients.
- Proportion of stroke patients at spoke hospitals treated with IVT who had an EQ-5D-5L utility score indicating good health.
- Proportion of stroke patients treated with EVT who had an EQ-5D-5L utility score indicating poor health at 3 months post-treatment, measured at hub, including direct to hub patients and spoke to hub patients.
- Proportion of stroke patients at spoke hospitals treated with IVT who had an EQ-5D-5L utility score indicating poor health.
- Proportion of stroke patients treated with EVT who had sICH. sICH is defined as intracerebral haemorrhage (parenchymal haematoma type 2 within 48 hours of treatment combined with neurological deterioration, leading to an increase of greater than or equal to 4 points on the NIHSS from baseline, or the lowest NIHSS value between baseline and 24 hours). This outcome will be assessed using de-identified data entered by sites into the eCRF. As standard clinical care, hospital staff collect follow-up data including the NIHSS score and assess if there is any haemorrhage on follow-up brain images up to 72 hours post-treatment.

eCRF, electronic case report form; EQ-5D-5L, Five-Dimension Health-Related Quality of Life Questionnaire, Five-Level version; EVT, endovascular thrombectomy; ICD-10, International Classification of Diseases, 10th Revision; IVT, intravenous thrombolysis; LVO, large vessel occlusion; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracerebral haemorrhage; TACTICS, Trial of Advanced CT Imaging and Combined Education Support for Drip and Ship.

Secondary outcomes: (comparing baseline with the 3–6 months postintervention phase)

The secondary outcomes include the proportion of good (mRS 0–2) and poor (mRS 5–6) outcome and EuroQoL (EQ-5D-5L) at 90 days post stroke (see box 1). Outcomes of good and poor functional status of patients treated with stroke reperfusion will be measured using the mRS[47] and the EuroQoL measure.[48] Both tools are extensively validated,[47 49] with evidence indicating good compliance at a national level in Australia.[48] As some participating sites may collect EuroQoL data using an earlier version (5-Dimension 3-Level version, EQ-5D-3L), a validated algorithm will be used to convert the EQ-5D-3L score into the EQ-5D-5L score.[50]

Process measures

Staff perceptions

Staff working in the assessment or treatment of acute stroke and leaders managing or leading care at participating hospitals will be invited to complete voluntary preintervention and postintervention surveys about perceptions of acute stroke care, stroke reperfusion and contextual elements of care including leadership. Eligible participants and preferred survey modality (eg, pen and paper or online) will be determined in consultation with the stroke coordinator at each site. Surveys will comprise validated measures[35 36 51–53] and tools used in a previous acute stroke implementation trial[54] and will take around 15 min to complete. Completion of the survey will be regarded as implied consent. Leaders and managers will be invited to provide additional feedback about implementation via semistructured qualitative individual interviews, conducted by a member of the research team with behavioural science expertise. Interviews will be conducted after written consent has been obtained. Feasibility, acceptability, experience and outcome of the virtual reality (VR) training will be specifically measured through pen and paper surveys and participant interviews preintervention and postintervention.

Level of engagement with study intervention

Engagement with study activities and elements will be assessed at the hospital and cluster level based on the approach used in the Thrombolysis ImPlementation in Stroke (TIPS) trial.[55] Engagement will include details such as the number of staff that attended each of the intervention activities (cluster workshop, cluster video-conferences, VR training module) and site completion of action planning.

Site readiness assessment of 'status quo' at baseline

The Organizational Readiness to Change Assessment instrument[56] and the transtheoretical stages of change model[57] highlight the importance of establishing levels of change readiness in order to optimise change efforts and improve implementation success. Site readiness will be measured via a voluntary group interview with stroke professionals at each hospital at the end of baseline, using a checklist format with variables derived from evidence-based time-saving strategies and stroke guidelines.[9 10 16] The checklist is a situational analysis of status quo. Interviews will be conducted by members of the research team with behavioural science expertise face to face or online and will be tape-recorded.

Intervention activities and elements

Behavioural framework underpinning trial design, roll-out and implementation

This protocol is presented in accordance with the 2013 Standard Protocol Items: Recommendations for Interventional Trials statement (see online supplemental file 2).

The reporting of trial results will be guided by the Standards for Reporting Implementation Studies[58] and the Template for Intervention Description and Replication[59] checklists. The TACTICS implementation intervention is based on the learnings from the TIPS trial,[55] concepts from the theoretical domains framework[60] and the principles of the COM-B (capability, opportunity, motivation and behaviour) approach.[61 62] The implementation intervention will be delivered by key stakeholders, opinion leaders and member of the research team with expertise in acute stroke care, advanced imaging, workflow optimisation and behaviour science at the individual, social and health system levels (see online supplemental file 3).

Implementation intervention

The target audience of the implementation intervention will be physicians and nursing leads (such as the site principal investigator and stroke coordinator) and relevant acute stroke workforce, herein referred to as the acute stroke access team (ASAT) at each hospital.

Implementation fidelity

To ensure relevance of the implementation intervention at each cluster, it is envisaged that the package will be tailored to better suit the cluster environment. Site assessments at baseline and the outcomes of the initial cluster workshop will assist with this. Emerging evidence points towards tailoring of interventions as a key factor for implementation success[63] without compromising fidelity,[64] as long as the underlying function of the intervention remains the same.[65]

In an effort to enhance implementation fidelity, the implementation intervention will be jointly delivered by members of the research team and the cluster coordinator (eg, hub site principal investigator), with support strategies and key stakeholders determined by discussion, prior to intervention roll-out. Cluster workshops will involve local representation from hospital executives, governance, ambulance and retrieval services, interventional experts, and quality improvement leaders.

Intervention strategies

Education regarding imaging use and interpretation

The intervention aims to improve the utilisation and interpretation of multimodal imaging (NCCT, computed tomography angiography (CTA), CTP). Didactic presentations and discussions during the cluster workshop (see online supplemental file 3) along with ad hoc troubleshooting (supported by the study team) will address the rationale behind multimodal imaging (CTA and CTP); utilisation of the AutoMIStar software; interpretation of multimodal imaging output; criteria relating to patient selection, based on core/penumbra maps and angiography to identify patients with high likelihood of good and poor response to IVT; and assessment of each site's current multimodal CT acquisition protocols by an experienced CT radiographer from the research team. The TACTICS VR acute stroke training module (described in section 'Clinician Training using VR' below) will also include core and penumbra imaging maps and angiography. For radiographers, the education will focus around how to produce good images, while education for clinicians will concentrate around knowledge and interpretation of images.

Systems improvement and workflow

Systems improvements will include provision of consensus clinical pathways and protocols towards optimal stroke reperfusion workflow, review of current cluster workflow, identifying gaps between current and ideal workflow, brainstorming around barriers and potential solutions, prioritising change effort based on feasibility and importance, developing an action plan, and monitoring progress by reviewing site-specific and cluster-specific processes and mechanisms, including progress towards action plan goals. This will occur during an interview (checklist format) to assess site readiness prior to the cluster workshop, activities during the cluster workshop and the post-workshop videoconferences (see online supplemental file 3).

Core elements will include process and pathway analysis, multimodal imaging, review of progress, VR acute stroke workflow optimisation tool, VR website of tools and resources, and the role of lead physicians, lead nurses and the ASAT in implementing change. Site-specific case scenarios, review and performance feedback regarding stroke reperfusion imaging and workflow processes, inter-hospital transfer arrangements, and action planning will be part of the cluster workshop and subsequent cluster videoconferences.

Clinician training using VR

The VR training programme will be based around the acute stroke hub and spoke reperfusion workflow, targeting junior and rotating staff, emergency department (ED) doctors and nurses, and radiographers at spoke hospitals. The modules include interactive scenarios where participants are asked to select answers from a list of multiple-choice questions at each stage of the stroke patient journey, with feedback provided along the way. At the end of the module, the participant will be provided with feedback on their performance. Staff will be supported and guided on the use of the VR training modules as part of the study intervention and will be encouraged to use the modules beyond the life of the project.

Take home kit

A take home kit will be provided by the research team during the 3-month study intervention phase to each hospital. Content includes TACTICS generic protocols and pathways, state-wide stroke reperfusion pathway, systems improvement resources and templates, details of available training options such as the Stroke Foundation online training modules in acute stroke care, an action planning template, stroke assessment support (NIHSS),

instructions relating to VR training, and change management training.

Activity 1

At the commencement of the intervention, a cluster workshop of 1–2 days will be delivered. The mode of delivery may vary (face to face and/or webinar) as per social distancing requirements due to COVID-19. The workshop will include didactic and interactive components. Site attendance will involve around three to four key representatives from each hospital, including a physician and a nurse lead, a representative from ED, and a radiographer or equivalent capacities. Enabling strategies include inviting hospital executives and representatives from stroke networks, systems improvement, and ambulance and retrieval services to attend the workshop and provide input and feedback on programme components.

Activity 2

The TACTICS VR acute stroke training module will be implemented at each site (hubs and spokes) following the cluster workshop.

Activity 3

Up to three cluster videoconferences will be delivered within each cluster following the workshop and within the 3-month intervention phase, focusing on site case review and feedback, problem solving, action planning, barriers and potential solutions.

Activity 4

Ad hoc meetings will be conducted to boost motivation and discuss issues relating to trial roll-out.

Tailoring of implementation intervention to the cluster environment

Tailoring will include how the package is rolled out in each cluster, based on preintervention assessments of the cluster environment. For example, cluster-specific resources will be available in the take home kit; local representation will be invited to the cluster workshop with workshop content tailored to reflect the cluster environment; the cluster coordinator will be invited to co-chair the problem solving cluster videoconferences following the cluster workshop; and sites will be (1) able to provide input into how the VR training modules are rolled out at their site, (2) asked to present case scenarios at cluster workshop and videoconferences, (3) encouraged to set challenging goals for improvements to stroke reperfusion care, and (4) encouraged to evaluate their goals based on importance and feasibility. Problem solving and feedback provided during the cluster videoconferences will be based on site-specific and cluster-specific challenges and solutions.

Planned adherence or fidelity will involve monitoring the number and type of staff at each site that engaged with the implementation intervention.

Sustainability of the implementation intervention will be emphasised throughout the trial. It is envisaged that the continued use of the VR programme and take home kit, along with site connections to local systems improvement expertise, will assist with sustainability.

Statistical methods

For the primary outcome, analysis will focus on complete cases. Clusters are the unit of intervention allocation and analysis.

Study endpoints

Primary outcome

The primary outcome (proportion of all stroke patients receiving EVT per cluster) will be analysed using a negative binomial mixed effects model, with site as a random effect and intervention as a fixed effect; a time variable will estimate any secular trends.

Secondary outcomes

Given the secondary outcomes are all proportions, the same analytic approach will be taken as with the primary outcome. No adjustment will be made to p values for the secondary outcomes given they have been specified a priori; instead, consistency of results across the good and poor outcomes as rated by mRS and EQ-5D-5L will be checked.

An interim analysis of the baseline prevalence rates will be performed in conjunction with the team statistician to check that they are in the range estimated in the sample size calculation. There will be no interim analysis of the effect of the intervention and hence no alpha spending function needed.

Sample size calculations and power

This six-cluster trial (each cluster consisting of one CSC and a minimum of three PSCs; ie, 38 hospitals in the trial overall) will accrue an overall denominator population of a minimum of 75 patients per month, or 225 patients for each 3-month preintervention and postintervention epoch, leading to 1350 patients in the 3-month preintervention period and an equal number in the 3-month postintervention period across all six clusters. Currently, the baseline rate of EVT implementation for the hub sites in scope for TACTICS is approximately 5% of all strokes, and the baseline rate of IVT implementation at the spoke sites in scope for TACTICS is approximately 5% of all strokes. Based on these assumptions, TACTICS will have 90% power to find an increase in EVT (primary outcome) from 5% during the preperiod to 8% in the postperiod, and 80% power to find an increase in IVT (secondary outcome) from 5% to 12.5%, at 5% significance, assuming an intraclass correlation coefficient of 0.05 (see table 1).

Ethics and dissemination

Ethical approval for the study has been obtained from the Hunter New England Human Research Ethics Committee (reference 18/09/19/4.13, New South Wales HREC reference HREC/18/HNE/241, Research Ethics Governance Information System approval number 2019/ETH01238) under a mutually accepted agreement for all

Table 1 Detectable postintervention proportion of EVT (primary outcome) and IVT (secondary outcome)

Baseline prevalence (%) (3 months)	% EVT (hub + spokes) postintervention (3 months)	% IVT (spokes only) postintervention (3 months)
2.5	5	
5	**8**	**12.5**
7.5	11	15.5

EVT, endovascular thrombectomy; IVT, intravenous thrombolysis.

sites. A collaborative research agreement has been signed between the University of Newcastle, Queensland Health, Boehringer Ingelheim, Apollo Medical Imaging Technology and Hunter New England Local Health District. The administrative institution for the trial is the University of Newcastle. The study has been registered with the University of Newcastle Research Information Management System (reference H-2019-0343) and ANZCTR and has obtained a Universal Trial Number via the WHO Clinical Trials Registry.

Trial outcomes will be disseminated widely via published manuscripts, conference presentations and at national and international platforms, including online education and training access on request, regardless of whether the trial was positive or neutral. Consent for publication is not applicable as the study only report de-identified data.

Availability of data and materials

The final data set will be available by contacting the corresponding author on reasonable request, and in accordance with ethical requirements and data access requirements stipulated by the data custodian (eg, Head of Data Sciences, Hunter Medical Research Institute). The data custodian will store the final data set in a data repository and will determine and monitor access to participant-level data and statistical code. Trial investigators and all research team investigators named on the ethics approval will have access to the trial data set.

Protocol amendments

Protocol amendments will be submitted for ethical approval and communicated via formal and informal mechanisms with site principal investigators, coordinators and the ASAT at each hospital. Amendments will also be noted on working group and steering committee agendas and minutes. Significant protocol amendments will be updated on the ANZCTR trial registration and reported in the final outcomes paper.

Data storage and confidentiality

Data will be stored, managed and archived according to the University of Newcastle, jurisdictional and National Health and Medical Research Council requirements. All information collected for this study will have identifying information removed, and will be kept private, confidential and secure. Transcripts from participant interviews will not include participant or hospital name, but will be linked with an ID to a spreadsheet which will be stored separately from the transcripts. No identifying data will be published.

DISCUSSION

There have been several improvements to acute stroke care in Australia since the approval of IVT for stroke, including recent imaging and EVT trials supporting imaging-guided decision making. However, despite the evidence base for implementing EVT, the infrastructure enabling linking of PSCs (especially those in regional and rural geographies) with CSCs, such as harmonised electronic medical records, imaging data system and coordinated interhospital transfer services, is still in its infancy in Australia. EVT is a highly specialised treatment requiring administration by a neurointerventionalist meeting society-mandated case volume criteria. Few physicians in Australia have these skills and thus EVT is mainly provided in larger metropolitan centres, leaving an equity gap in the provision of best evidence acute stroke care for regional and rural Australians.

Previous trials have shown that it is possible to improve access to evidence-based acute stroke care, while few trials have been rigorously tested in regional and rural settings spanning a large geographical area. Large trials such as the Stroke123 improvement trial[66] used financial incentives and quality improvement methodology to improve adherence to acute stroke guidelines in the Australian state of Queensland; the USA-based Get With The Guidelines trial[67] focused on systems improvement using champions and collaborative meetings; a prospective German trial[68] used simulation training to shorten process times in regional areas; and the Spanish Transfer to the Local Stroke Center versus Direct Transfer to Endovascular Center of Acute Stroke Patients with Suspected Large Vessel Occlusion in the Catalan Territory (RACECAT) trial[69] used a prehospital intervention to test whether a direct to mothership approach was superior to a drip and ship model of care for patients with a potential LVO. It is challenging to implement and sustain changes in complex health systems over time, although noted to be possible at a national and international level in a variety of health settings,[70] particularly if the design, implementation and evaluation consider the context in which the intervention is delivered.[71] The results of the recent RACECAT trial support the appropriateness of a drip and ship approach and highlight the importance of good workflow arrangements as demonstrated by rapid DIDO times.[72]

The TACTICS trial is testing the effectiveness of an implementation intervention, comprising immersive VR technology, best evidence multimodal imaging and acute stroke workflow protocol and pathway resources, embedded within existing or emerging infrastructure, tailored to the cluster environment, which is being delivered in close liaison with doctors, nurses, radiographers,

interventionalists, management, stroke networks, government agencies and academic stakeholders.

The evidence generated from the TACTICS trial has the potential to enhance access to best practice acute stroke care, particularly in regional and rural Australia, while embedding successful change efforts into codesigned and agreed protocols, pathways, processes and infrastructure, using a hub and spoke model of care, supported by health service executives and state-based governing structures. The VR training module may improve access to novel professional development and education in regional and rural Australia, impacting on clinical confidence, job satisfaction and staff retention. This study has the potential to guide future implementation efforts in complex health systems with its rigorous design, outcome measures and tailored implementation approach.

Sustainability

Participating hospitals will be left with a support package (eg, take home kit) of tools and resources and the VR training module. Sites will be encouraged to keep using these resources beyond the life of the trial. It is envisaged that designated EVT CSCs (hubs) will continue to work with PSCs (spokes) to sustain collaboration and structures around stroke reperfusion care, including collaboration around imaging review and interhospital transfer of EVT patients. The additional linking with local and state-wide systems improvement capability throughout the study intervention is envisaged to facilitate continuous engagement with quality improvement processes.

Study limitations and challenges

Target audience being smaller centres without established stroke research culture

This trial is innovative in its design and includes predominantly smaller hospitals without an established research culture. Many centres have a small acute stroke workforce with staff covering a range of duties and hospitals within the region. They seldom have established acute stroke teams and are predominantly run by a senior physician with stroke expertise, a part-time stroke coordinator, and ED staff including rotating, junior and visiting medical officers. This makes system improvements difficult both to establish and sustain.

Intervention allocation being sequentially allocated, not blinded

As the implementation of EVT hub and spoke models of care is at an early stage in Australia, random allocation of the study intervention will not be feasible within the timeframe of the study, therefore introducing potential selection bias.

External factors

Factors that are beyond the control of this study include the roll-out of telestroke network structures in Australia, changes to national-level and state-level policies, guidelines or performance measures for stroke, and any changes to national training or data capture registries underlying training and data collection mechanisms for this study. New evidence in acute stroke care may also be rolled out during the trial period which cannot be controlled. However, with a controlled design, thoroughly tested package intervention, capturing of contextual elements of care preintervention and postintervention, and a comprehensive roll-out strategy underpinned by theoretical and behavioural theory, this trial is anticipated to provide valuable insights into further implementation work in complex health systems.

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imaging education. SK assisted with site recruitment, contracts and agreements. FRW, RJH, SM and AK oversaw the development and internal testing of the VR training application and ongoing technical support. JA and CO provided conceptual advice on data collection, study design, statistical analysis and power calculations. AM assisted with meeting documentation and data elements. LH and CD assisted with site recruitment and data elements. AR, CLP, OW, MC and CRL were part of the writing group for the manuscript. All authors read and approved the final manuscript.

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Competing interests Boehringer Ingelheim is the manufacturer of the tissue plasminogen activator (tPA) drug and thus has an interest in the study. They, however, have no right to publish any results arising from this trial.

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