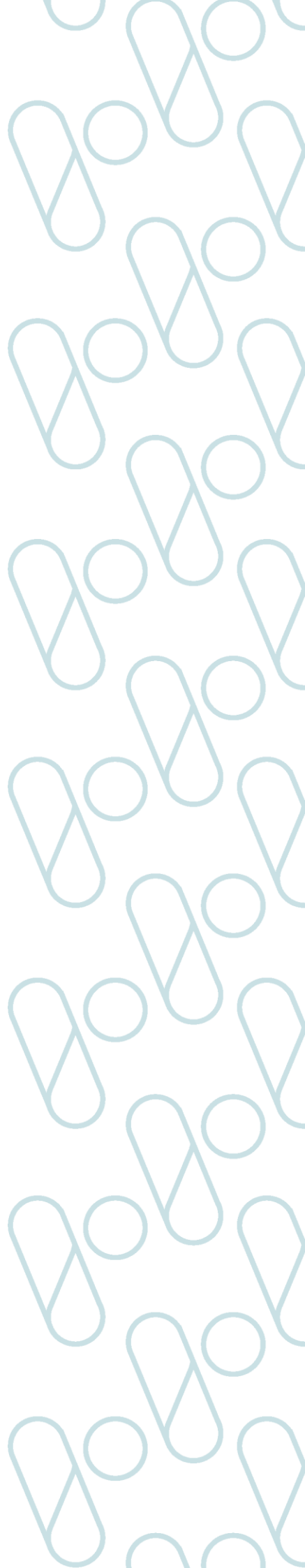


**October 2018**

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# Endovascular clot retrieval for acute stroke

Statewide service protocol for Victoria



## ABBREVIATIONS

AuSCR	Australian Stroke Clinical Registry
AV	Ambulance Victorian Government
ALS	Advanced Life Support
ARV	Adult Retrieval Victoria
bpm	beats per minute
CT	computed tomography
CTA	computed tomography angiography
CTP	computed tomography perfusion
DSMC	Data Safety Monitoring Committee
ECG	electrocardiogram
ECR	endovascular clot retrieval (endovascular thrombectomy/mechanical thrombectomy)
ED	emergency department
eGFR	estimated Glomerular Filtration Rate
FAST	Face, Arms, Speech, Time
GCS	Glasgow Coma Scale
ICA	internal carotid artery
IM/IV	intramuscular/intravenous
MASS	Melbourne Ambulance Stroke Scale
MCA	middle cerebral artery
MICA	Mobile Intensive Care Ambulance
MMC	Monash Medical Centre
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
NIHSS	National Institutes of Health Stroke Scale
PACS	picture archive and communication system
RMH	Royal Melbourne Hospital
VST	Victorian Stroke Telemedicine (program)
WARS	Weight, Access, Rankin, Suitability

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# About this document

This document outlines the Victorian approach to providing endovascular clot retrieval (ECR), a highly effective treatment that reduces the occurrence of disability and death in some patients who have had an ischaemic stroke.

This protocol was first developed by the Department of Health and Human Services in 2016.

In response to new evidence, Safer Care Victoria's Stroke Clinical Network led a review of the protocol in 2018. This updated protocol was developed through broad consultation and takes advantage of the substantial local expertise and infrastructure, including the Victorian Stroke Telemedicine (VST) program and the Australian Stroke Clinical Registry (AuSCR).

We would like to acknowledge Associate Professor Bruce Campbell and Associate Professor Peter Hand who led the development and revision of the protocol.

For full acknowledgements, see page 15.

## What's new?

- Management protocol for patients identified as potential candidates for ECR therapy **6 to 24 hours** after stroke onset.
- Imaging requirements for patients to be considered for ECR in the **6 to 24 hour** window after stroke onset.
- Process for transferring patients to a statewide ECR centre, including duties and responsibilities of all care providers.

## Key contacts

### VST

03 9035 7188

### Ambulance Victoria

000 (with a 15-minute response requested)

### Royal Melbourne Hospital ECR team

1300 ECR RMH (1300 327 764)

### Monash Medical Centre

1300 ECR MMC (1300 327 662)

# Introduction

Stroke is a leading cause of death worldwide and a leading cause of disability. About 80 per cent of strokes are ischaemic, with the remainder due to various types of bleeding into the brain. Ischaemic stroke results from a blocked artery (or vessel occlusion) causing reduced blood flow to regions of the brain. Treatments to restore blood flow can reduce disability for stroke survivors.

## Intravenous thrombolysis

Intravenous thrombolysis dissolves blood clots and has been used to treat ischaemic stroke since the late-1990s. It is an effective treatment, reducing disability in patients who respond. Studies have shown that intravenous thrombolysis is unable to rapidly break down the larger clots that cause the most devastating strokes.

## Endovascular clot retrieval

Endovascular clot retrieval (ECR) is the removal of large clots occluding a brain vessel through an intra-arterial approach. ECR is a highly effective treatment that reduces the occurrence of disability and death after an ischaemic stroke.<sup>1–5</sup> When combined with intravenous thrombolysis (or alone in patients ineligible for thrombolysis), ECR can result in up to 70 per cent of patients recovering.

For more evidence about ECR, see page 13.

## Delivering ECR in Victoria

Victoria has two statewide ECR centres which provide a 24-hour, seven-day service for patients from across the state. The Royal Melbourne Hospital was the first, followed by Monash Medical Centre in late 2017.

Health systems have established rapid pathways to:

- identify the appropriate patient
- arrange brain imaging
- review the brain imaging results
- communicate with a neurointerventionist
- transfer the patient to the angiography suite for treatment.

This can be challenging, even within a single hospital.

## About ECR

**ECR is a time-critical treatment** and best results are achieved when blood flow is restored quickly – that is, when time from stroke onset to reperfusion is minimal.

**Specialised skills are required to perform ECR.** It is technically challenging and performed by highly trained radiologists, neurologists or neurosurgeons who have specialist skills in neurointervention.

**ECR is only available at some tertiary hospitals.** Centralising services allows for greater procedural volume, experience and staff training.<sup>6</sup> This leads to better patient outcomes with fewer complications.

**ECR requires a well-organised system** to identify suitable candidates and rapidly transport them to an ECR-capable centre. This relies on close cooperation and integrated care between ECR neurointerventionists and multidisciplinary stroke unit teams.



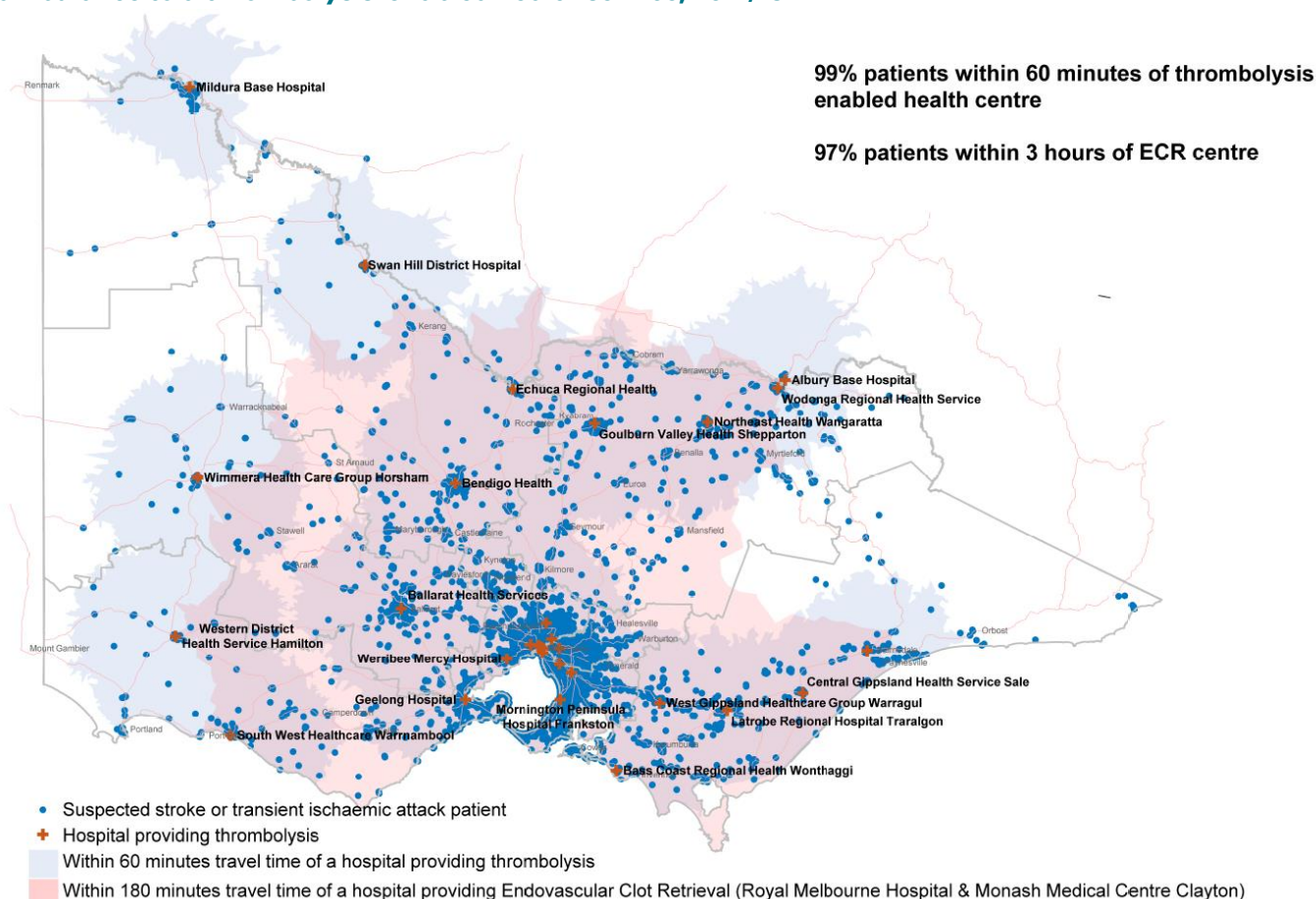
## Supporting services to deliver high-quality care

To help regional and rural health services develop area-specific strategies, Safer Care Victoria's Stroke Clinical Network released the **Framework for regional acute stroke services** in 2013.<sup>7,8</sup> Health services now have agreed protocols and procedures to facilitate rapid transfer of suspected patients with acute stroke to reperfusion and stroke unit-capable centres.

This work is augmented by the VST program, which helps rural and regional centres identify suitable patients for thrombolysis and ECR. Now fully implemented, VST provides telemedicine connection to specialist stroke physicians for 17 key regional health services. These sites would not otherwise have access to this specialist advice.<sup>9,10</sup>

Current estimates suggest that more than 99 per cent of suspected stroke patients in Victoria are within a 60-minute ambulance journey of a health service with capability to provide intravenous thrombolysis. Now with two ECR centres, 97 per cent will be within a three-hour road journey from an ECR centre.

**Figure 1: Suspected stroke or transient ischaemic attack patients within 60 minutes travel time by ambulance to a thrombolysis-enabled health service, 2017/18**



Source: Ambulance Victoria

# Protocol for ECR delivery

This protocol outlines the pathway for assessment and referral for ECR. It also details the roles and responsibilities of the local clinician, the VST stroke physician, the ECR centre stroke physician and the neurointerventionist.

ECR requires health service systems to provide a coordinated response across the patient journey.

## 1. Identify the right patient

- Arrange and review rapid brain imaging including computed tomography (CT) perfusion and angiography
- Provide thrombolysis where appropriate

## 2. Refer patient to ECR

- Communicate with a neurointerventionist
- Liaise with Ambulance Victoria to arrange urgent transfer

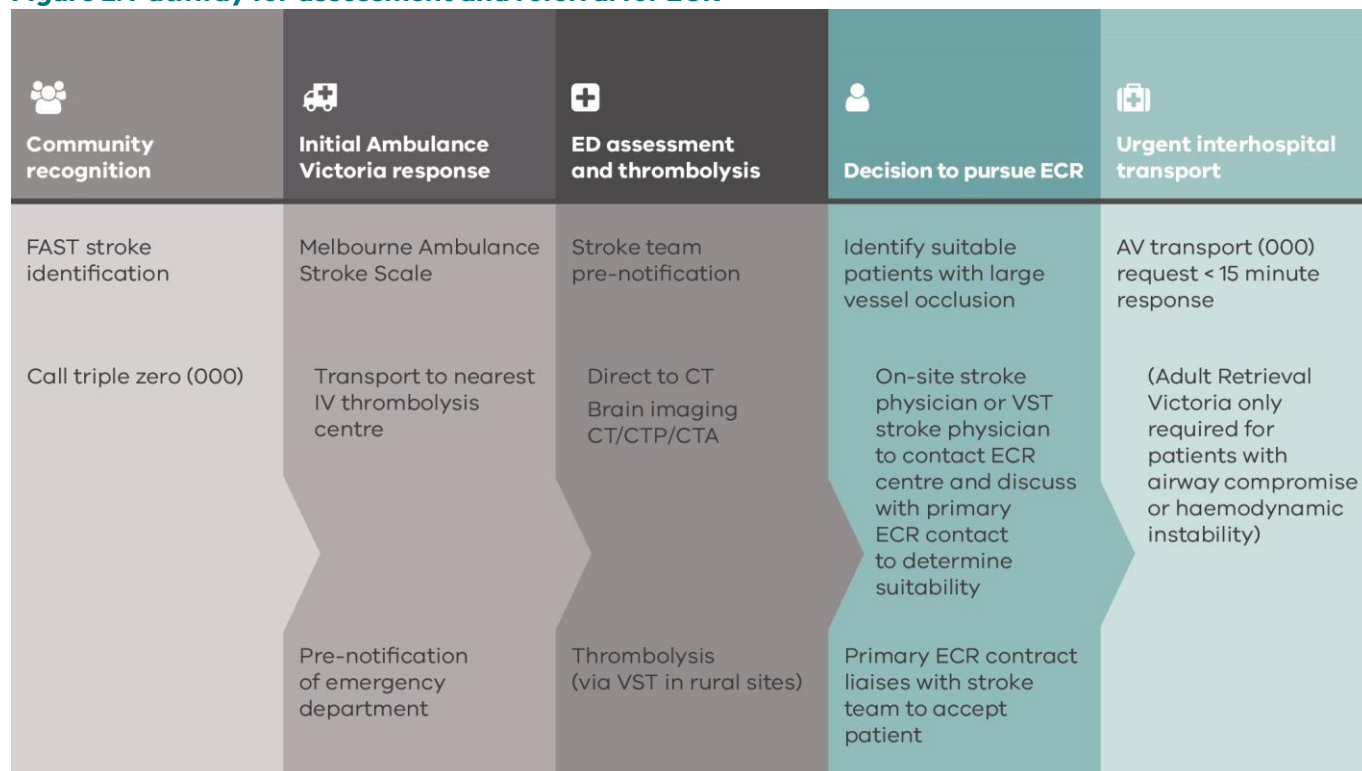
## 3. Transfer the patient for treatment

- Expedite transfer to the nearest ECR centre
- Get the patient to the angiography suite for treatment
- Start ECR as soon as possible

## 4. Manage the patient after ECR

- Monitor neurological status and vascular access sites for complications
- Consider repatriating patient to their local stroke service

**Figure 2: Pathway for assessment and referral for ECR**



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## 1. IDENTIFY THE RIGHT PATIENT

A patient whose stroke symptoms started within **4.5 hours** may be a candidate for intravenous thrombolysis.

A patient with a stroke due to a large vessel occlusion is a potential candidate for both intravenous thrombolysis and ECR, with ECR suitable for selected patients **up to 24 hours** after the time they were last seen well.

Patients who are ineligible for intravenous thrombolysis may still be candidates for ECR.

### Community recognition

Patients with suspected stroke can be rapidly identified in the community using the Face, Arms, Speech, Time ('FAST') approach leading to a triple zero (000) call.<sup>11</sup>

### Ambulance Victoria response

Ambulance Victoria paramedics apply the Melbourne Ambulance Stroke Screen (MASS)<sup>12</sup> to diagnose suspected stroke.

The pre-hospital focus is on:

- rapid transport to the nearest thrombolysis-equipped stroke centre (see **Appendix 1**)
- pre-notification of the receiving emergency department (ED) with clinical details including the patient's name, date of birth and stroke onset time.

### ED assessment

Rapid assessment should occur immediately on arrival in the ED.

The stroke team should have already received notification of the patient's imminent arrival so staff can meet the patient and (preferably) directly transfer them on the ambulance trolley to the CT scan.

For patients potentially suitable for reperfusion therapies **within 24 hours** of the last known well time, routine brain imaging should include (see Panel 1):

- a non-contrast CT brain
- CT perfusion (if there is no intracerebral haemorrhage)
- computed tomography angiography (CTA) from the aortic arch to the vertex.

If there is any doubt about the appropriate imaging protocol, please discuss this as early as possible with the on-site or VST stroke physician.

### Intravenous thrombolysis

To avoid delays, administer intravenous thrombolysis to eligible patients in parallel with CT perfusion/angiography acquisition and ECR decision making.

## Panel 1: Brain imaging for suspected stroke

### Non-contrast CT brain

Diagnoses intracerebral haemorrhage, established ischaemic stroke, mimics (such as a tumour), subtle early ischaemic changes and hyperdense thrombus in the arteries

Note: In addition to standard thick axial slices, thin (~1 mm) slices improve detection of hyperdense thrombus and should be a standard reconstruction

### CT perfusion

Improves diagnostic sensitivity for ischaemic stroke

Note: reperfused stroke may have normal CT perfusion. CT perfusion has limited sensitivity for lacunar stroke

Indicates brain tissue viability (extent of irreversible injury and tissue at risk)

- Essential for treatment beyond **6 hours** after the time last known to be well
- Increases appropriate use of intravenous thrombolysis for mild/'rapidly improving' patients with occlusion
- Prognostic and reduces the incidence of futile ECR

### CT angiogram (aortic arch to brain vertex)

Provides immediate knowledge of carotid stenosis and proximal vasculature

Provides critical information regarding vascular access if considering transfer for ECR

For intracerebral haemorrhage, CTA can demonstrate underlying structural vascular abnormality requiring intervention and risk of ongoing haematoma enlargement – 'spot sign' representing contrast extravasation

When to perform CT perfusion and angiography:

- time of onset (last seen well) within **24 hours**
- potentially disabling clinical deficit
- do not wait for creatinine results. If there is known kidney disease with eGFR < 30 mL/min consider risk-benefit and use IV normal saline hydration if proceed with contrast.<sup>13</sup>

CT contrast is OK if the patient is already on haemodialysis

Consider risk-benefit and premedication if history of contrast allergy



## 2. REFER PATIENT TO ECR

### Decision to pursue ECR

Rapid decision making regarding thrombolysis and identification of large vessel occlusion is required to detect patients potentially suitable for ECR.

#### Panel 2: Guidelines for ECR eligibility

- Ischaemic stroke with proven large vessel occlusion on CTA
  - internal carotid artery (ICA)
  - middle cerebral artery (MCA)
    - M1 segment – between the carotid terminus and MCA bifurcation
    - Proximal M2 segment – with significant clinical and perfusion deficit
  - basilar artery
- Independent premorbid function (modified Rankin scale score 0–2). The assessment of premorbid function should consider social and domestic interactions, such as independence in banking, shopping and driving
- Time window: when the procedure can be commenced within **6 hours** of stroke onset, broad clinical and imaging criteria should be applied. Basilar artery occlusion may be treated up to **24 hours** after onset. Anterior circulation patients with favourable CT perfusion imaging should receive ECR up to **24 hours** after stroke onset, as per current national/international guidelines<sup>14–17</sup>
- Intravenous thrombolysis commenced if eligible
- Accessible to clot retrieval – assessment by neurointerventionist (requires remote picture archiving and communication system (PACS) access at all referral sites)

### ‘Out of guidelines’ intervention

Patients who do not fully meet these guidelines may still be considered for ECR but will be considered to have the procedure ‘out of guidelines’. This may be considered for presentations with:

- modified Rankin scale score  $\geq 3$
- proximal M2 occlusion with small clinical and/or perfusion deficit
- any distal occlusion site.

The ECR interventionist makes the final clinical decision to perform the intervention.

Patients who receive treatment ‘out of guidelines’ should have their case presented at the next reperfusion monitoring committee meeting for discussion.

## Role of referring medical team

### For metropolitan hospitals

- Arrange rapid brain imaging
- Administer intravenous thrombolysis as appropriate
- Call the primary ECR contact as early as possible (consultant led +/- conference call including registrars) and ensure imaging is immediately accessible to the receiving clinician

**Royal Melbourne Hospital** primary contact **1300 ECR RMH** (1300 327 764)

If after **5 minutes** it has not been possible to speak with the primary contact, call the hospital's stroke neurologist on call for ECR (call RMH switch doctor direct 9342 8989)

**Monash Medical Centre** primary contact **1300 ECR MMC** (1300 327 662)

If after **5 minutes** it has not been possible to speak with the primary contact, call the centre's stroke neurologist via the switchboard (MMC switch 9594 6666)

- Arrange transport and expedite transfer via Ambulance Victoria, guided by primary contact
- Explain to the patient/relatives that the inter-hospital transfer is for the consideration of ECR but that the final decision on suitability for the procedure will be made on arrival at the ECR centre. Provide written educational materials to the patient and their family
- Send/transfer the appropriate clinical documentation related to the patient

### For VST-enabled sites

- Call VST as early as possible, including pre-hospital notification of high-probability ECR patients
- Arrange rapid brain imaging and make it immediately accessible to the VST stroke physician
- Administer intravenous thrombolysis as appropriate
- Arrange transport and expedite via Ambulance Victoria (with Adult Retrieval Victoria support where appropriate), guided by a VST or ECR centre stroke physician
- Explain to the patient/relatives that the inter-hospital transfer is for the consideration of ECR but that the final decision on suitability for the procedure will be made on arrival at the ECR centre. Provide written educational materials to the patient and their family
- Send/transfer the appropriate clinical documentation related to the patient

## Metropolitan hospitals

Hospitals without on-site ECR availability should initiate a direct call between the referring consultant (which may also involve the on-site registrar) and the primary ECR contact. Metropolitan centres acting as non-designated ECR providers will default to this pathway if they are unable to provide ECR locally.

If the referrer is unable to speak to the primary contact within **5 minutes** they should initiate contact with the secondary contact.

## VST-enabled hospitals

For the 17 regional hospitals supported by VST, the VST stroke physician will help identify likely ECR candidates and advise on transport requirements. They will then liaise with the primary ECR contact to confirm ECR suitability.

### Role of the VST stroke physician

- Undertake audiovisual consult to fully assess the patient and communicate with the patient's family/carers
- Diagnose and advise on suitability for intravenous thrombolysis
- Assess CT/computed tomography perfusion (CTP)/CTA and potential ECR eligibility: 'WARS' – Weight, Access (vascular), Rankin (premorbid), Suitability (other co-morbidities, is GA possible etc).
- If not suitable for reperfusion treatment, can advise on other management options (for example, hemicraniectomy, intracerebral haemorrhage management)
- Call the primary ECR contact to determine suitability for transfer

#### **Royal Melbourne Hospital** primary contact **1300 ECR RMH** (1300 327 764)

If after **5 minutes** it has not been possible to speak with the primary contact, call the hospital's stroke neurologist on call for ECR (call RMH switch doctor direct 9342 8989)

#### **Monash Medical Centre** primary contact **1300 ECR MMC** (1300 327 662)

If after **5 minutes** it has not been possible to speak with the primary contact, call the centre's stroke neurologist via the switchboard (MMC switch 9594 6666)

- Provide advice on the best transport option for the patient to be transported to the ECR centre
- Communicate with the ECR stroke physician for every case, following a decision to transfer, so the ECR centre can organise a bed
- Send documentation of the consultation to the referring hospital

### 3. TRANSFER THE PATIENT FOR TREATMENT

#### Transport considerations

The primary ECR contact or VST stroke physician will determine which level of transport is appropriate based on the clinical condition of the patient.

#### Ambulance Victoria

The vast majority of stroke patients require standard ambulance transport with Advanced Life Support (ALS) level paramedics.

The referring centre should initiate a time-critical, inter-hospital Ambulance Victoria transfer via a triple zero (000) call. Request a less than **15-minute response** to elicit a code 1 (lights and sirens) response.

Ambulance Victoria will determine the fastest mode of transport for the time-critical transfer of patients. This may be via road, helicopter, fixed-wing aircraft or a combination of the above based on current conditions and resources.

The threshold for intubation for air transport is lower than that for road transport, and this may influence the choice of transport mode. For Air Ambulance transportation the flight paramedic will directly contact the receiving ECR centre via the 1300 number to give an update on expected time of arrival, and the patient's clinical status.

#### Adult Retrieval Victoria

Some situations may require discussion with Adult Retrieval Victoria (ARV). These include:

- reduced consciousness (a significantly reduced Glasgow Coma Score (GCS) not due to aphasia)
- agitation requiring sedation or intubation
- respiratory compromise requiring intubation
- haemodynamic instability.

Clinically, these patients are likely to have a basilar artery occlusion or a massive hemispheric infarct.

The referring centre should initiate contact with ARV, on the advice of the VST on call or on-site stroke physician. Mobile Intensive Care Ambulance (MICA) paramedics will likely be assigned to these cases after the ARV consult and ARV will then coordinate the patient's transfer.

#### Preparing for transfer

To minimise delays, the patient must be ready to transport, including all necessary transfer documentation.

- Ensure the remaining dose of thrombolysis is prepared and connected without the need for paramedics to change syringes and so on.
- Routine intubation is not required for transport of patients with anterior circulation ischaemic stroke, whether by road or air.
- Studies indicate that general anaesthesia may be associated with a worse patient outcome.<sup>18</sup>
  - When GA is required maintain BP > 140 mmHg systolic.<sup>19-21</sup>
- GCS has limited utility in assessing airway function in stroke and should not be used for this purpose.
- Intracerebral haemorrhage and basilar occlusion have a different risk profile and may require intubation for transport.

In some cases the same paramedic crew who transported the patient to hospital may still be available to transport the patient to the ECR centre after rapid assessment in the CT scanner.

See **Appendix 2** for an information sheet to help ambulance paramedics when a thrombolysis infusion is ongoing during transport. This avoids the need for a hospital nurse or doctor to accompany the patient.

### Notifying receiving ECR centre

The patient's registration details should be faxed to the receiving ECR centre to allow medical records to be prepared.

Provide an updated estimated time of arrival to the receiving ECR centre when the patient leaves and again approximately **45 minutes** prior to arrival for longer transfers.

### Management at the ECR centre

The stroke team should meet the patient on arrival and escort them directly to the angiography suite unless there is cardiorespiratory instability requiring stabilisation in the ED.

Imaging may not need to be repeated unless there has been a significant change in clinical status or unexpected extended delay in transportation leading to concern about safety of ECR therapy.

Performing the procedure with the support of the anaesthetic team, either awake +/- conscious sedation or under general anaesthesia at the discretion of the ECR neurointerventionist. Careful monitoring of the patient's blood pressure to prevent hypotension is critical.<sup>19-21</sup>

### Role of the primary ECR contact

- Liaise with the external referring Stroke or VST physician to determine suitability for transfer
- If necessary, liaise with local ECR stroke physician to alert the in-hospital team

### Role of the ECR stroke physician

- Arrange a bed by alerting the in-hospital medical team
- Provide post-procedural medical management

### Role of the ECR neurointerventionist

- Review imaging to assess suitability for ECR and plan the procedure
- Coordinate team availability to perform the procedure
- Make the final decision regarding an ECR procedure when the patient arrives at the ECR centre
- Perform and document the procedure



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## 4. MANAGE THE PATIENT AFTER ECR

### Post-procedure care and return to referring centre

Following ECR, the patient would generally remain at the ECR centre for **24 hours** for post-procedure monitoring and repeat brain imaging.

Recommended post-procedure observations are similar to post-thrombolysis observations, with the addition of arterial access site and limb vascular observations:

- half-hourly for six hours
- one-hourly for four hours
- two-hourly for 12 hours
- four-hourly until reviewed.

### Reportable observations

- Hypertension  $\geq 185/110$  – consider why this has occurred (could there be raised intracranial pressure?)
- Hypotension  $< 100$  systolic – consider retroperitoneal or other bleeding
- New tachycardia ( $> 100$  bpm)
- Any evidence of bleeding (apart from bruising) including at the arterial access site
- Any change in neurological state, including new/increasing weakness and deterioration in conscious state (hospital medical officer must review the patient and discuss with registrar/consultant)
- Allergic reaction
- Fevers

Patients requiring inpatient rehabilitation should be transferred to their local acute stroke unit. It is an expectation of centres referring patients to the ECR centre that they will accept the return of patients within **24 hours** of the request by the ECR centre. It is expected that the bed managers at referring sites will prioritise repatriation of these patients to the original referring site.

All patients undergoing intervention at an ECR centre will be reviewed by the treating neurointerventional team as part of the post-operative process.

Stroke clinic follow up should be individualised depending on clinical need and patient choice. This may occur at the local stroke unit or at the ECR centre (in person or via telemedicine).

For patients who make sufficient recovery to be discharged directly home, the stroke allied health team, where appropriate/required, will arrange follow up with the relevant disciplines in the patient's local area.

# The evidence

## ECR IS A HIGHLY EFFECTIVE TREATMENT

In 2015 there were five positive randomised trials of ECR published in the *New England Journal of Medicine*.<sup>1-5</sup> These trials firmly established ECR as standard care for patients with ischaemic stroke due to large artery occlusion within **6 hours** of stroke onset. Subsequently, the publication of the DAWN<sup>22</sup> and DEFUSE 3<sup>23</sup> trials in 2018 extended the time window for ECR to **24 hours** in selected patients with favourable brain imaging using CT perfusion or magnetic resonance imaging (MRI).

The positive trials followed the publication in 2013 of three neutral randomised trials (IMS-3,<sup>24</sup> SYNTHESIS<sup>25</sup> and MR-RESCUE<sup>26</sup>). There were three key differences between the positive trials and these older studies:

1. The use of more effective stent retriever devices essentially doubled the rate of successfully opening the blocked artery.
2. Treatment was faster.
3. CT or magnetic resonance angiography (MRA) was used to confirm there was a large vessel occlusion. In addition most of the recent trials excluded patients with large regions of irreversibly injured brain tissue.

The first positive trial of ECR was the Multicenter Randomized CLinical trial of Endovascular treatment for Acute ischaemic stroke in the Netherlands (MR CLEAN), a 500 patient Dutch study that randomised patients with large vessel ischaemic stroke to ECR using a range of devices (82% stent retrievers) versus standard care (which included intravenous alteplase in 89 per cent of cases).<sup>1</sup> Patients were treated up to **6 hours** after stroke onset. At three months post-stroke there was a highly significant reduction in overall disability, with 33 per cent of ECR versus 19 per cent of control patients achieving independence. These results prompted Data Safety Monitoring Committees (DSMC) to review the ongoing clinical trials evaluating thrombectomy in acute ischaemic stroke.

Overwhelming benefit was demonstrated in the EXTEND-IA, ESCAPE and SWIFT PRIME trials and further recruitment into these trials was ceased.

EXTEND-IA randomised 70 patients in Australia and New Zealand to intravenous alteplase versus alteplase plus ECR using the Solitaire stent retriever.<sup>2</sup> Patients were treated up to **6 hours** after stroke onset. Computed tomography (CT) perfusion imaging was used to identify patients with definite large vessel occlusion and salvageable brain tissue (irreversibly injured ischaemic core < 70 mL). At three months post stroke there was a highly significant reduction in overall disability, with 71 per cent of ECR versus 40 per cent of alteplase-only patients achieving independence.

ESCAPE recruited 315 patients from Canada, the United States and Korea. The inclusion window was longer – up to **12 hours** after symptom onset and the protocol employed grading of collateral blood flow using CTA to exclude patients with a large area of irreversibly injured brain.<sup>3</sup> A range of devices were used (79 per cent stent retriever, 61 per cent Solitaire device), and 76 per cent received intravenous alteplase. At three months post stroke there was a highly significant reduction in overall disability, with 53 per cent of ECR versus 29 per cent of control patients achieving independence.

SWIFT PRIME recruited 196 patients from North America and Europe. The design was similar to EXTEND-IA, with all patients receiving intravenous alteplase and device use restricted to the Solitaire device.<sup>4</sup> The protocol initially employed perfusion imaging with a maximum core volume of 50 mL, but this was made optional during the course of the trial. At three months post stroke there was a highly significant reduction in overall disability, with 60 per cent of ECR versus 35 per cent of control patients achieving independence.

Subsequent to these results the REVASCAT trial was terminated by the DSMC due to the loss of equipoise.<sup>5</sup> This trial, performed in four Catalanian centres, recruited 206 patients up to **8 hours** after symptom onset and used only the Solitaire device. Seventy-three per cent received intravenous alteplase. Patients with a large area of irreversibly injured brain on non-contrast CT were excluded. At three months post stroke there was a significant reduction in overall disability, with 44 per cent of ECR versus 28 per cent of control patients achieving independence.

Further trials were reported in 2016. The THRACE trial showed similar results to MR CLEAN in a relatively unselected group of patients.<sup>27</sup> The PISTE<sup>28</sup> and THERAPY<sup>29</sup> trials (which were terminated early in the recruitment phase) showed similar trends that did not reach statistical significance.

In 2017 the DAWN trial reported strong treatment benefit in patients **6 to 24 hours** after the time they were last known to be well using clinical-core mismatch selection with CT perfusion or MRI. The full results were published in January 2018,<sup>22</sup> shortly before the publication of the DEFUSE 3 trial<sup>23</sup> in patients **6 to 16 hours** after the time they were last known to be well. DEFUSE 3 used broader criteria (essentially an ischaemic core volume < 70 mL) which included ~60 per cent more patients than DAWN criteria. DEFUSE 3 patients who would not have been DAWN eligible had the same treatment effect as those who were DAWN eligible. Virtually all DAWN-eligible patients would also be DEFUSE 3 eligible (i.e. the DAWN population is almost completely a subset of the DEFUSE 3 population). Grouped together, approximately half of the patients in these trials who received ECR returned to functional independence compared to ~15 per cent in the control group.

There was no evidence of reducing treatment effect as time elapsed if imaging remained favourable but it is crucial to recognise that the proportion of patients with favourable imaging declines rapidly with time – those further from time of event were less likely to meet ECR criteria.

## ECR IS TIME CRITICAL

The relationship between shorter delays to intravenous alteplase administration and improved patient outcome is well known.<sup>30</sup> Similar relationships have been reported for ECR.<sup>31-32</sup> This reflects the expansion of irreversible injury into the previously salvageable 'ischaemic penumbra' as time passes. Therefore every effort to minimise the onset to reperfusion time must be made. The ESCAPE trial achieved very fast workflow through a continuous quality improvement and feedback process.

Lessons learned from alteplase quality improvement programs<sup>32-34</sup> also apply to ECR. Key elements of such systems are pre-hospital notification by ambulance personnel, a coordinated stroke team response in the ED, direct transport to a CT scan on an ambulance stretcher, prioritisation of brain imaging and direct transfer to an angiography suite.

The strongly positive results of the pivotal trials have led to a change in international stroke guidelines in Australia, the United States, Canada and Europe.<sup>14-17</sup> All now recommend ECR as the standard of care for patients with ischaemic stroke due to large vessel occlusion within **6 hours** of stroke onset using broad selection criteria. Beyond **6 hours**, guidelines recommend ECR in patients who have favourable CT perfusion or MRI profiles as used in the DAWN and DEFUSE 3 trials. Provision of ECR is in accordance with the Australian acute stroke clinical care standard, Quality Statement Two – Time Critical Treatment.<sup>2</sup>

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## ACKNOWLEDGEMENTS

Development and revision of the protocol was led by Associate Professor Bruce Campbell and Associate Professor Peter Hand.

We thank all those involved in the first edition of the protocol.

For the second edition, we also thank members of the Stroke Clinical Network's Reperfusion committee for their input and support.

### **Reperfusion committee (as of October 2018)**

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Dominique Cadilhac (Data Custodian, AuSCR and Head Public Health Stroke Division, Florey Institute of Neuroscience and Mental Health)

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Ashu Jhamb (Director of Neurointervention, St Vincent's Hospital Melbourne)

Richard Gerraty (Director of Stroke, Epworth Health Care)

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# Appendix 1: Metropolitan and regional hospitals providing thrombolysis

## METROPOLITAN THROMBOLYSIS CENTRES (JUNE 2018)

Austin Hospital  
Box Hill Hospital  
Cabrini Hospital Malvern  
Epworth Richmond  
Frankston Hospital  
Monash Medical Centre, Clayton Campus  
St Vincent's Hospital  
Sunshine Hospital  
The Alfred  
The Northern Hospital  
The Royal Melbourne Hospital

## REGIONAL THROMBOLYSIS CENTRES (JUNE 2018)

Albury Wodonga Health, Albury Campus  
Ballarat Health Services  
Bairnsdale Regional Health Service  
Bass Coast Health, Wonthaggi  
Bendigo Health Care Group  
Central Gippsland Health Service, Sale Hospital  
Echuca Regional Health  
Goulburn Valley Health, Shepparton  
Hamilton Base Hospital  
Latrobe Regional Hospital, Traralgon  
Mildura Base Hospital  
Northeast Health Wangaratta  
South West Healthcare, Warrnambool  
Swan Hill District Health  
University Hospital Geelong  
Werribee Mercy Hospital  
West Gippsland Hospital, Warragul  
Wimmera Health Care Group, Horsham



# Appendix 2: Ambulance information sheet for patients receiving IV thrombolysis

This patient has received intravenous thrombolysis for stroke

## Dose

☐ **ALTEPLASE** 0.9 mg/kg (max 90 mg) 10% as bolus, 90% as intravenous infusion

Over one hour

Infusion rate for this patient =

Please run until infusion complete

☐ **TENECTEPLASE** \_\_\_mg given as bolus over 10 seconds

## Observations

Monitor electrocardiogram (ECG) for heart rate increase, external signs of bleeding, GCS deterioration, which might indicate bleeding

Discuss with clinician if reduction in conscious state (management = rapid transport to destination)

## Potential adverse effects

### Bleeding (~2–5%)

Systemic (such as epistaxis)

Intracerebral

#### Management

Standard first aid for external bleeding

Cease infusion if still running and non-compressible bleeding

Rapid transport to destination

### Orolingual angioedema (~1%)

Usually only half of tongue and lips swollen

#### Management

Stop alteplase infusion if still running

Nebulised 5 mg adrenaline in 5 mL normal saline if airway compromised, which is rare. Avoid IM/IV adrenaline due to risk of inducing severe hypertension

Call for MICA backup

Rapid transport to destination

If the patient continues to deteriorate the crew must consult with the 'control room clinician' prior to administering IV adrenaline. Care needs to be taken to exclude haemorrhage as a cause of the patient's deterioration

If the clinician requires further information regarding the patient they may contact the VST stroke physician (details on the clinician database)

**Advise the receiving hospital via the control room when approximately 45 minutes from arrival**

# Appendix 3: AuSCR reperfusion minimum dataset in Victoria

This is the current AuSCR minimum dataset for monitoring reperfusion (thrombolysis and ECR) in participating Victorian health services. This version (published 25 July 2018) may be subject to minor changes over the course of the program life. Note, AuSCR has multiple data collection program options and not all these variables are collected in each AuSCR Program.

For further information please see [www.auscr.com.au](http://www.auscr.com.au) or contact [admin@auscr.com.au](mailto:admin@auscr.com.au).

## AT REFERRING HOSPITAL

Variable	Response set
NIHSS at baseline	Number: 0-42, 99
Did the patient have a brain scan after this stroke?	Yes/No
Date of first brain scan after the stroke	DDMMYYYY
Time of first brain scan after the stroke	hh:mm
Not documented	True/False
Date of subsequent brain scan after the stroke	DDMMYYYY
Not applicable (no further scans)	True/False
Time of subsequent brain scan after the stroke	hh:mm
Not documented	True/False
Was a stroke telemedicine consultation conducted?	Yes/No/Unknown
Did the patient receive intravenous thrombolysis?	Yes/No/Unknown
Date of delivery	DDMMYYYY
Time of delivery	hh:mm
Was there a serious adverse event related to thrombolysis?	Yes/No
Type of adverse event	Intracranial haemorrhage
	Extracranial haemorrhage
	Angioedema
	Other

## ACUTE PHASE AT RECEIVING HOSPITAL/ECR CENTRE

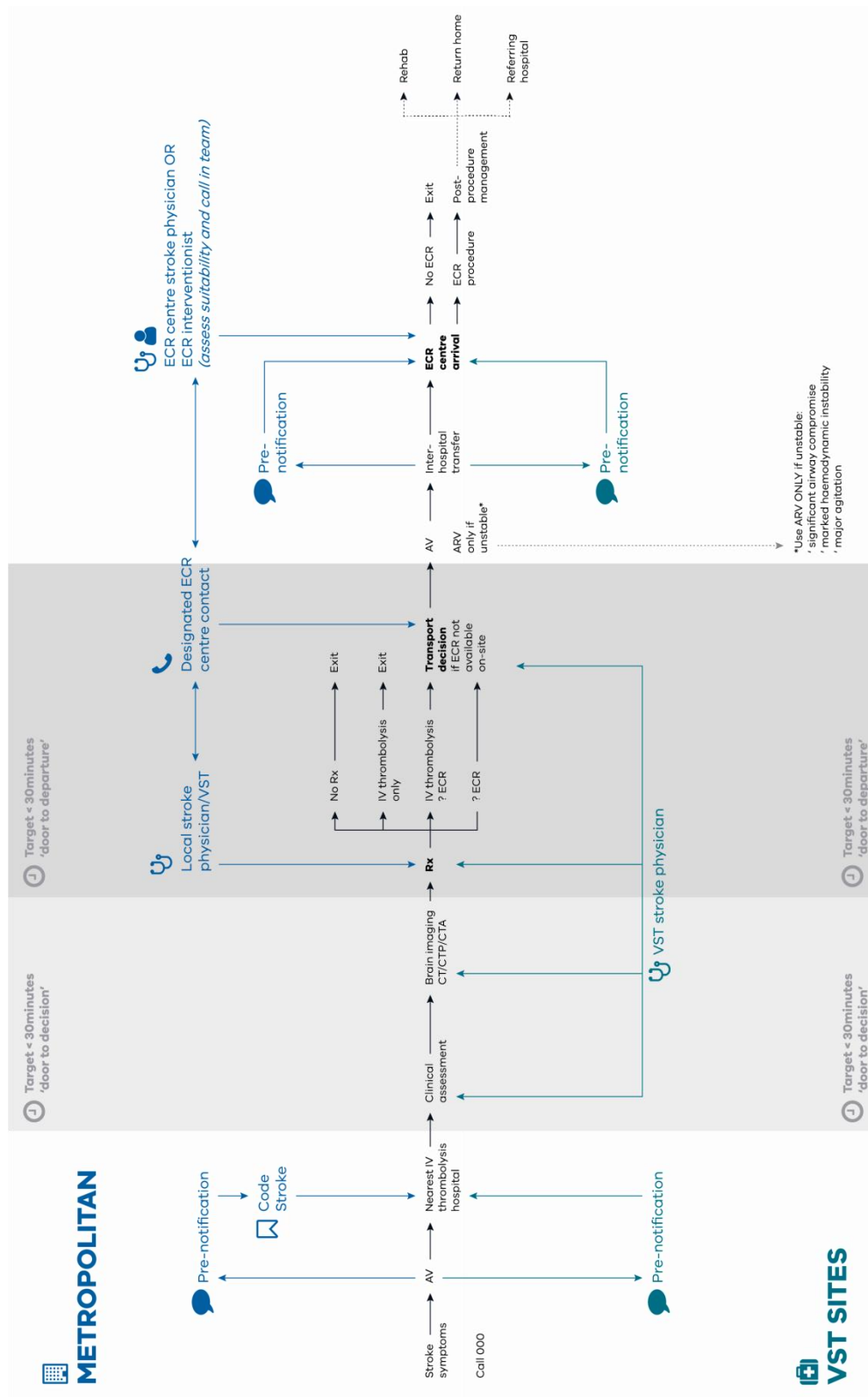
Variable	Response set
<b>Direct admission to hospital (bypass ED)</b>	Yes/No
<b>Was the patient transferred from another hospital?</b>	Yes/No/Unknown
<b>What was the reason for transfer?</b>	Yes/No to all reasons
Need for intravenous thrombolysis	
Need for stroke unit care	
Need for rehabilitation	
Need for brain imaging only	
Need for ICU	
Need for specialist medical assessments	
Need for specialist surgical interventions	
Need for diagnostic tests	
Need for coordinated care by a stroke service	
Need for endovascular therapy	
Unknown	
Other (specify)	
<b>Date of subsequent brain scan after the stroke</b>	DDMMYYYY
Not applicable (no further scans)	True/False
<b>Time of subsequent brain scan after the stroke</b>	hh:mm
Not documented	True/False
<b>Time of subsequent brain scan after the stroke</b>	hh:mm
Not documented	
<b>Was other reperfusion (endovascular) treatment provided?</b>	Yes/No
<b>Treatment date for other reperfusion</b>	DDMMYYYY
<b>NIHSS before endovascular treatment</b>	Number: 0–42, 99
<b>Time groin puncture</b>	hh:mm
<b>Time of completing recanalisation/procedure</b>	hh:mm
<b>Final eTICI (thrombolysis in cerebral infarction score)</b>	0, 1, 2a, 2b, 2c, 3
<b>Acute occlusion sites</b>	True/False to all occlusion sites
Left	ACA
Right	PCA
ICA-EC	BA
ICA-IC	VA
MCA-M1	No occlusion
MCA-M2	Not documented
MCA-M3	Other

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## 24-HOUR DATA AT RECEIVING HOSPITAL/ECR CENTRE

Variable	Response set
24-hour NIHSS	Number: 0-42, 99
Was there haemorrhage within the infarct on follow-up imaging?	Yes/No/Unknown
Details of haemorrhage	HI1: small petechiae/ HI2: more confluent petechiae/ PH1: 30% of the infarcted area with mild space-occupying effect/ PH2: 30% of the infarcted area with significant space-occupying effect

# Appendix 4: Statewide flow diagram of ECR pathway





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