Safer Care Victoria

April 2024

Endovascular thrombectomy 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
DH	Department of Health
DSMC	Data Safety Monitoring Committee
ECG	electrocardiogram
EVT	endovascular thrombectomy/mechanical thrombectomy (prev. – endovascular clot retrieval - ECR
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 archiving 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 (EVT), 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 (DH) in 2016 and revised in 2018 due to the emergence of new evidence relating to the management protocol for patients identified as potential EVT candidates, and the imaging requirements for patients to be considered for EVT in the 6–24-hour window after stroke.

In May 2023, further evidence was published in the Stroke Foundation s Australian and New Zealand Living Guideline for Stroke Management. In response to this, Safer Care Victoria conducted a subsequent review of the protocol in June 2023.

We would like to acknowledge the Associate Professor Benjamin Clissold, the Safer Care Victoria Cardiovascular Learning Health Network and the Acute Stroke Community of Practice, who have led the latest protocol revision. We also acknowledge Professor Bruce Campbell and Associate Professor Peter Hand who led the protocol development and 2018 review.

For full acknowledgements, see page 16.

What's new?

- Information regarding the management of large core ischaemic stroke within **24 hours** of stroke onset.
- Information regarding the structure, collaborative and integrated approach to managing EVT in Victoria including additional services provided by Austin Health and Alfred health

This document is intended for clinicians working in health care settings, not for the general public.

If you, or someone you are caring for, are experiencing signs or symptoms of stroke, **call Triple Zero (000) immediately.**

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 survivor

Intravenous thrombolytics

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

Endovascular clot retrieval

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

For more evidence about EVT, see page 13

Delivering EVT in Victoria

Victoria current has five EVT centres.

The Royal Melbourne Hospital and Monash Medical Centres operate as DH designated statewide EVT referral centres for patients who initially present to a non-EVT capable centre and who meet criteria for thrombectomy.

The Austin and Alfred hospitals provide independent 24/7 EVT services within their local catchment. St Vincent's provides 24/7 EVT services to its local catchment in conjunction with The Austin Hospital.

At times of high demand, both The Austin and The Alfred assist the DH designated statewide referral centres by operating as a co-operative network.

Services to Victorians in remote and regional areas are coordinated through VST.

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 EVT

EVT is a time-critical treatment and best results are achieved when blood flow is restored as quickly as possible – that is, when time from stroke onset to reperfusion is minimised.

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

EVT is only available at some tertiary hospitals. Centralising services allows for greater procedural volume, experience and staff training.[6] This leads to better patient outcomes with fewer complications.

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

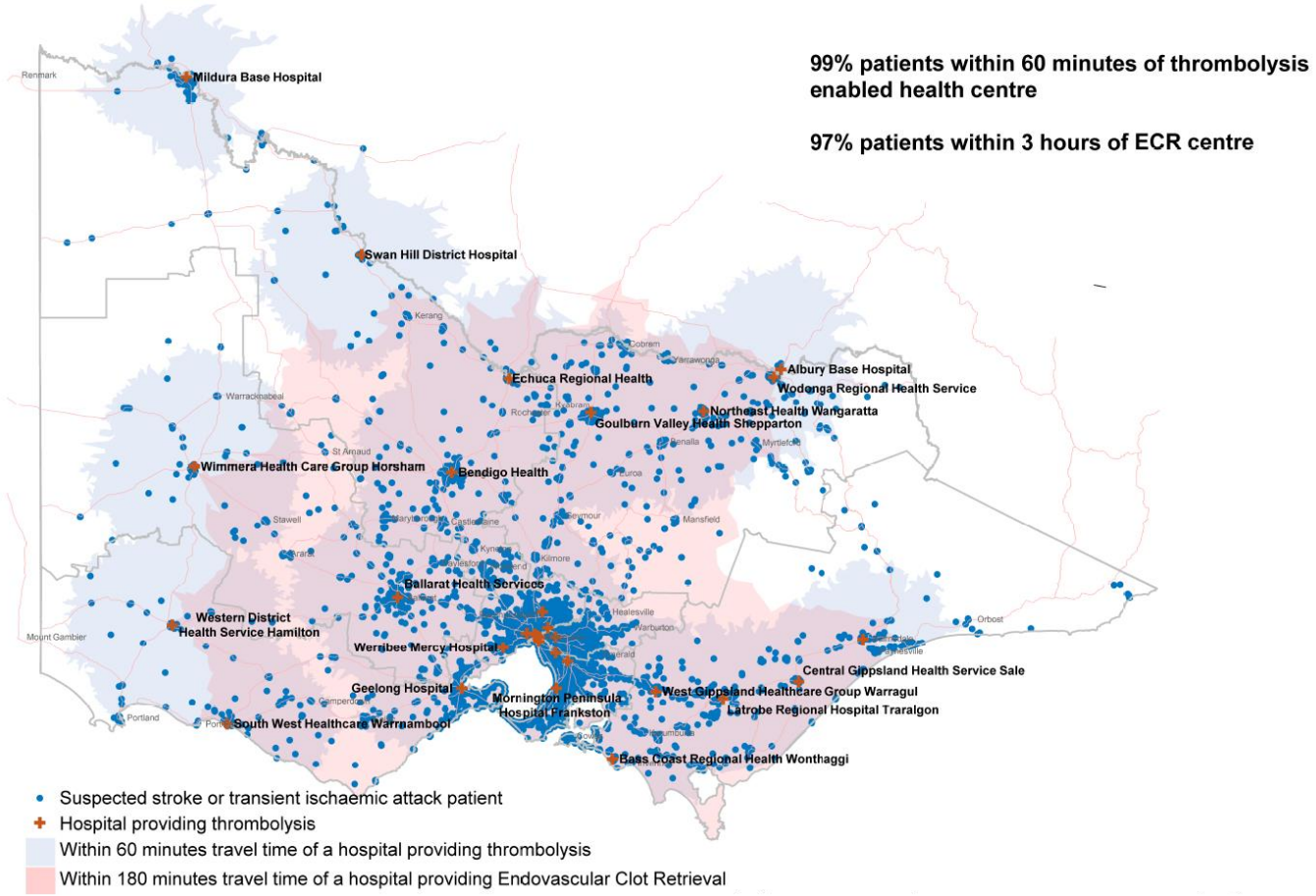
Supporting services to deliver high-quality care

To help regional and rural health services develop area-specific strategies, the Stroke Clinical Network released the **Framework for regional acute stroke services** in 2013.[7,8] 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 thrombolytics and EVT. Now fully implemented, VST provides telemedicine connection to specialist stroke physicians for 19 key regional health services in Victoria and 2 in Tasmania. These sites would not otherwise have access to this specialist advice.[9,10]

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 thrombolytics and 97 per cent are within a three-hour road journey from an EVT centre.

Figure 1: Suspected stroke or transient ischaemic attack patients within 60 minutes travel time by ambulance to a thrombolytic-capable health service, 2017/18 – Additional sites not represented below are Portland District Health and Wodonga Hospital.



Source: Ambulance Victoria

Protocol for EVT delivery

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

EVT 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 thrombolytics where appropriate
2. **Refer patient to EVT**
   - Communicate with a neurointerventionist
   - Liaise with Ambulance Victoria to arrange urgent transfer
3. **Transfer the patient for treatment**
   - Expedite transfer to the nearest EVT centre
   - Get the patient to the angiography suite for treatment
   - Start EVT as soon as possible
4. **Manage the patient after EVT**
   - 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 EVT

1. IDENTIFY THE RIGHT PATIENT

A patient whose stroke symptoms started within **4.5 hours** may be a candidate for intravenous thrombolytics, regardless of whether EVT is planned.

For patients experiencing an ischaemic stroke with potentially disabling outcomes and fulfil both the standard clinical and perfusion mismatch criteria, intravenous thrombolytic should be administered up to **9 hours** after the patient was last seen to be well or from the midpoint of sleep for patients who wake with stroke symptoms. This may not apply if immediate EVT is planned.[35]

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

Patients who are ineligible for intravenous thrombolytics may still be candidates for EVT.

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.[11]

Ambulance Victoria response

Ambulance Victoria paramedics apply the Melbourne Ambulance Stroke Screen (MASS)[12] to diagnose suspected stroke.

The pre-hospital focus is on:

- rapid transport to the nearest thrombolytic-capable stroke centre or rendezvous with a mobile stroke unit (See **Appendix 1**).
- In some regions, a severity-based ambulance triage tool may be used to directly transport patients to an EVT-capable centre.
- 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 scanner.

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 thrombolytics

To avoid delays, administer intravenous thrombolytics to eligible patients in parallel with CT perfusion/angiography acquisition and EVT 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 thrombolytic treatment beyond **4.5 hours** after the time last known to be well
- Increases appropriate use of intravenous thrombolytics for mild/rapidly improving' patients with occlusion
- Prognostic and reduces the incidence of futile EVT

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 EVT

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.[13]

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 EVT

Decision to pursue EVT

Rapid decision-making regarding thrombolytics and identification of large vessel occlusion is required to detect patients potentially suitable for EVT.

Panel 2: Guidelines for EVT eligibility

- Ischaemic stroke with proven large vessel occlusion on CTA
  - internal carotid artery (ICA)
  - middle cerebral artery (MCA) (M1 segment and proximal or dominant M2 segments)
  - basilar artery
  - tandem occlusion of both the cervical carotid and intracranial large arteries.
- 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
- Consideration should be given to the extent and location of brain injury, frailty, comorbidities, and the patient's and/or family 's wishes
- Time window: up to 24 hours from the time the patient was last known to be well, as per current national/international guidelines[14-17]
- Eligible stroke patients should receive intravenous thrombolytics while concurrently arranging endovascular thrombectomy
- Accessible to clot retrieval – assessment by neurointerventionist (requires remote picture archiving and communication system (PACS) access at all referral sites)
- Patients presenting beyond 24hrs after they were last seen well may be considered for endovascular thrombectomy if imaging suggests the presence of salvageable brain tissue

'Out of guidelines' intervention

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

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

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

Patients who receive treatment 'out of guidelines' should be reviewed internally at a health service level through established clinical governance committees.

Role of referring medical team

For metropolitan hospitals

- Arrange rapid brain imaging
- Administer intravenous thrombolytic as appropriate
- Call the primary contact at a DH designated statewide EVT referral centre as early as possible (consultant led +/- conference call including registrars) and ensure imaging is immediately accessible to the receiving clinician
- 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 EVT but that the final decision on suitability for the procedure will be made on arrival at the EVT 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
- Arrange rapid brain imaging and make it immediately accessible to the VST stroke physician
- Administer intravenous thrombolytics as appropriate
- Arrange transport and expedite via Ambulance Victoria (with Adult Retrieval Victoria support where appropriate), guided by a VST or EVT centre stroke physician
- Explain to the patient/relatives that the inter-hospital transfer is for the consideration of EVT but that the final decision on suitability for the procedure will be made on arrival at the EVT 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 EVT availability should initiate a direct call between the referring consultant (which may also involve the on-site registrar) and the primary contact at DH designated statewide EVT referral centre. Metropolitan centres will default to this pathway if they are unable to provide EVT 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 19 regional hospitals supported by VST, the VST stroke physician will help identify likely EVT candidates and advise on transport requirements. They will then liaise with the primary contact at DH designated statewide EVT referral centre to confirm suitability.

Role of the VST stroke physician

- Undertake audio-visual 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 EVT 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 contact at DH designated statewide EVT referral centre to determine suitability for transfer

  Royal Melbourne Hospital

  If after **5 minutes** it has not been possible to speak with the primary contact, call the hospital's stroke neurologist on call for EVT.

  Monash Medical Centre

  If after **5 minutes** it has not been possible to speak with the primary contact, call the centre's stroke neurologist via the switchboard.
- Provide advice on the best transport option for the patient to be transported to the EVT centre
- Communicate with the EVT stroke physician for every case, following a decision to transfer, so the EVT centre can organise a bed
- Send documentation of the consultation to the referring hospital

3. TRANSFER THE PATIENT FOR TREATMENT

Transport considerations

The primary contact at a DH designated statewide EVT referral centre 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 EVT 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 thrombolytic 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.
- Some studies indicate that general anaesthesia may be associated with a worse patient outcome.[18.]
  - When GA is required maintain BP > 140 mmHg systolic.[19-21]
- 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 EVT centre after rapid assessment in the CT scanner.

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

Notifying receiving EVT centre

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

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

Management at the EVT 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 EVT therapy.

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

Role of the primary contact at DH designated statewide EVT referral centre

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

Role of the EVT stroke physician

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

Role of the EVT neurointerventionist

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

4. MANAGE THE PATIENT AFTER EVT

Post-procedure care and return to referring centre

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

Recommended post-procedure observations are similar to post-thrombolytic 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 ≥ 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 EVT centre that they will accept the return of patients within **24 hours** of the request by the EVT centre. It is expected that the bed managers at referring sites will attempt to prioritise repatriation of these patients to the original referring site over local emergency department pressures.

All patients undergoing intervention at an EVT 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 EVT 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

EVT IS A HIGHLY EFFECTIVE TREATMENT

In 2015 there were five positive randomised trials of EVT published in the *New England Journal of Medicine*.[1–5] These trials firmly established EVT 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[22] and DEFUSE 3[23] trials in 2018 extended the time window for EVT 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,[24] SYNTHESIS[25] and MR-RESCUE[26]). 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 EVT 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 EVT using a range of devices (82% stent retrievers) versus standard care (which included intravenous alteplase in 89 per cent of cases).[1] 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 EVT 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 EVT using the Solitaire stent retriever.[2] 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 EVT 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.[3] 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 EVT 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.[4] 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 EVT 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.[5] This trial, performed in four Catalonian 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 EVT 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.[27] The PISTE[28] and THERAPY[29] 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,[22] shortly before the publication of the DEFUSE 3 trial[23] 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 EVT 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 EVT criteria.

Trials published in 2022 and 2023 demonstrate positive outcomes from EVT 0-24 hours after onset for patients with a broader range of imaging characteristics. Large core studies showed trends to increased symptomatic intracerebral haemorrhage and vascular complications in some but not all. The SELECT-2 trial showed a higher occurrence of early neurological decline, possibly due to increased oedema post infarct, though the overall positive impact on functional recovery was clear.

Yoshimura et al conducted a multicentre randomised trial in Japan in 2022, involving patients with occlusion of large cerebral vessels and sizable strokes on imaging – as indicated by Alberta Stroke Program Early Computed Tomographic Score (ASPECTS) value of 3 to 5. Patients with large cerebral infarctions had better functional outcomes with endovascular therapy than with medical care alone though had more intracranial haemorrhages.[36]

In 2023, Sarraj et al performed a randomised international trial involving patients with stroke due to occlusion of the internal carotid artery, or first segment of the middle cerebral artery to assess EVT within 24hours of onset. Patients had an extensive ischaemic core (defined as ASPECTS value 3 to 5 or at least 50 ml core volume on CTP or MRI). The trial was stopped early for efficacy at interim analysis. Better functional outcomes resulted from EVT than medical care with 20% of patients in the EVT group and 7% in the medical care group achieving functional independence. [37]

In April 2023, Huo et al published a study analysing the treatment of acute large-vessel occlusion in the anterior circulation within 24 hours from the time they were last known to be well with EVT and medical management versus medical management alone. (ASPECTS 3 to 5 or infarct

core volume of 70-100ml). Following the second interim analysis, the trial was stopped early owing to efficacy, as patients with large cerebral infarctions had better outcomes with EVT within 24 hours than with medical management alone. A shift of score on the mRS towards better outcomes was observed in favour of EVT over medical management group. [38]

Although these trials expand the criteria for EVT treatment, particularly 6-24 hours, the rates of functional independence and independent ambulation in patients with >100mL core are relatively low and the individual patient attitude towards disability, frailty and comorbidity needs to be considered.[35]

EVT IS TIME CRITICAL

The relationship between shorter delays to intravenous alteplase administration and improved patient outcome is well known.[30] Similar relationships have been reported for EVT.[31-32] 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[32-34] also apply to EVT. 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 changed international stroke guidelines in Australia, the United States, Canada and Europe.[14-17] Provision of EVT is in accordance with the Australian Acute Stroke Clinical Care Standard, Quality Statement Two – Time Critical Treatment.[2]

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Appendix 1: Metropolitan and regional hospitals providing thrombolytics

METROPOLITAN THROMBOLYTIC-CAPABLE CENTRES (AUGUST 2023)

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 THROMBOLYTIC-CAPABLE CENTRES (JUNE 2023)

Albury Wodonga Health, Albury and Wodonga Campuses

Grampians (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

Portland District Health

South West Healthcare, Warrnambool

Swan Hill District Health

University Hospital Geelong

Werribee Mercy Hospital

West Gippsland Hospital, Warragul

Wodonga Hospital

Wimmera Health Care Group, Horsham

Appendix 2: Ambulance information sheet for patients receiving IV thrombolytics

This patient has received intravenous thrombolytic 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** 0.25mg/kg, up to maximum total dose of 25mg, 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 (thrombolytics and EVT) 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** or contact **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

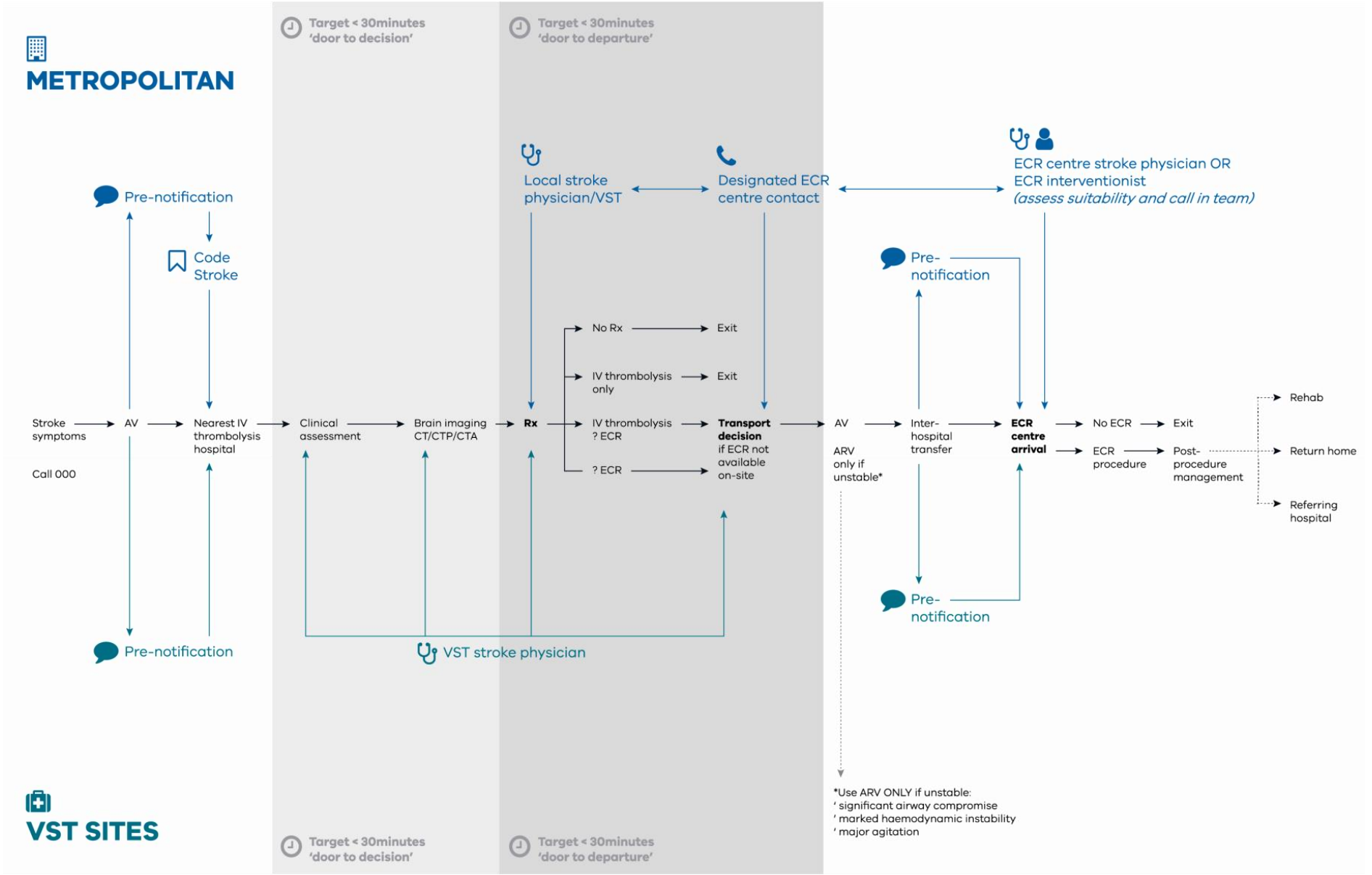
ACUTE PHASE AT RECEIVING HOSPITAL/EVT CENTRE

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

24-HOUR DATA AT RECEIVING HOSPITAL/EVT 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 EVT pathway



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